Institut für Molekulare Mechanismen bei Krankheiten
der Vetsuisse-Fakultät Universität Zürich

Direktor: Prof. Dr. med. vet et phil. II Michael Hottiger

Musculoskeletal Research Unit (MSRU)
Leiterin: Prof. Dr. med. vet. Brigitte von Rechenberg, Dipl. ECVS

Arbeit unter wissenschaftlicher Betreuung von
Salim Darwiche, PhD

Evaluating the efficacy of DYNACORD™ suture

Inaugural-Dissertation

zur Erlangung der Doktorwürde
der Vetsuisse-Fakultät Universität Zürich

vorgelegt von

Martina Heygen

Tierärztin

aus Frankfurt am Main, Hessen, DE

genehmigt auf Antrag von

Prof. Dr. med. vet. Brigitte von Rechenberg, Referentin

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Meiner Familie
in Liebe und Dankbarkeit

Zusammenfassung

Rotatorenmanschettenrupturen sind ein häufiges muskuloskeletales Problem und Auslöser für chronische und behindernde Schulterschmerzen. Die Komplikationsrate bei Operationen ist mit bis zu 90% enorm hoch und führt zu unzufriedenstellenden klinischen Ergebnissen. Hauptursache für das Scheitern solcher Operationen an der Rotatorenmanschette ist die Re-Ruptur. Ein wichtiger Faktor, welcher maßgeblich den Erfolg von Operationen an der Rotatorenmanschette bedingt, wird dem hierfür eingesetzten Nahtmaterial zugeschrieben.

Diese Dissertation stellt eine Studie vor, welche die chirurgische Versorgung einer partiellen Ruptur der Infraspinatussehne im Schafmodell untersuchte. Ziel dieser Studie war die Erforschung der Wirksamkeit eines neuen Nahtmaterials „Dynacord™“ im Vergleich zu dem üblicherweise für Korrekturen der Schultersehnenruptur verwendeten Fiberwire® Nahtmaterial. Hierfür wurden die biomechanischen Eigenschaften der geheilten Infraspinatussehne nach Korrektur mittels Dynacord™ oder Fiberwire® getestet. Des Weiteren wurde der Heilungsverlauf durch eine makroskopische Evaluation des geheilten Sehnengewebes analysiert. Die Resultate der Studie zeigen vergleichbare Ergebnisse in Klinik und Biomechanik für mit Dynacord™ und Fiberwire® behandelte Tiere. Die makroskopische Evaluation hingegen zeigte weniger Abnormalitäten im Heilungsverlauf der Sehne nach Behandlung mit Dynacord™ . Nach Zusammenfassung der klinischen, makroskopischen und biomechanischen Daten dieser Studie kann bestätigt werden, dass das Dynacord™ Nahtmaterial eine potentielle Alternative für die chirurgische Versorgung der Rotatorenmanschettenruptur darstellt.

Summary

Rotator cuff tears are a common musculoskeletal problem causing chronic and disabling shoulder pain. With a failure rate of up to 90% the rate of complications through re-tearing is relatively high and the clinical outcome unsatisfying. An important factor affecting the success of the surgery is thought to be related to the suture material used for rotator cuff repair. This thesis presents a study performed in a rotator cuff repair model in sheep, specifically of a partially transected infraspinatus tendon. The study was conducted to demonstrate the efficacy of a newly developed suture material „Dynacord™“ in comparison to the commonly used Fibrewire® suture material selected for rotator cuff repair in clinics. The main goal was to compare the biomechanical strength of the healed infraspinatus tendon following the repair with either Dynacord™ or Fibrewire®. Furthermore, the macroscopic healing response of the tendons triggered by the two suture materials was also assessed.

The results of the study showed equivalent clinical and biomechanical outcome for sheep treated with Dynacord™ or Fibrewire®. However, macroscopic evaluation demonstrated less abnormalities in tissue healing response for Dynacord™- treated animals. When clinical, macroscopical and biomechanical results from the study were combined, the new Dynacord™ suture material was proven to be a valuable and attractive alternative for rotator cuff repair.

1 Introduction

Shoulder pain is one of the main musculoskeletal problems leading patients to vist their physician. Up to 70% of these patients suffer from rotator cuff disease[1,2] being the most common soft tissue injury in the shoulder, which is predominant in the elderly population[3,4]. Next to the physical pain, suffering from rotator cuff tendinopathy includes stiffness in the shoulder and movement disability which affects a person`s ability to carry out daily activities and work[1]. Without surgical treatment there is a risk of delayed or failed healing, functional loss of the affected muscle and injuries in surrounding tissue[5,6]. Even with surgical repair there is still a high postoperative failure rate because of retearing and there is little evidence that the outcomes of rotator cuff repair are improving[7]. Most of the surgeries are not successful, which often results in re-operating. The failure rate can rise up to 95%, depending on severity of the disease and other factors[8-10]. To increase the healing rate of rotator cuff repair, more research is essential. Next to the surgical technique, the material used in the surgery is crucial for the result[11].

1.1 Purpose of study

This thesis presents a study performed in a rotator cuff repair model in sheep, specifically the repair of a partially transected infraspinatus tendon. The study was conducted to demonstrate the efficacy of the Dynacord™ suture, a newly developed suture material, in comparison to predicate Fibrewire® suture that is commonly used in rotator cuff repair. The main goal was to compare the biomechanical strength of the healed infraspinatus tendon tissue following the repair with either Dynacord™ or Fibrewire®. Furthermore, there interest was also placed in evaluating the macroscopic healing response of the tendons triggered by the two suture materials.

1.2 Thesis structure

To understand the nessecity of the study, the backround about rotator cuff repair will be explained. This includes the anatomy of the rotator cuff, information about rotator cuff tears, the biological and biomechanical characteristics of tendon tissue healing, the current treatment options, the problems related to these treatments and the explanation as to why a sheep model was used. In the following section there will be a detailed report about the current study, including materials and methods as well as the results. The results will then be discussed.

2 Background

2.1 Anatomy of rotator cuff

The glenohumeral joint is the articulation between the shallow glenoid cavity of the scapula and the round head of the humerus. That kind of joint is described as a „ball and socket joint“. As there is a limited interface between these two articulating bones, this is an inherently unstable connection[12-16]. There are different musculoskeletal components which provide stability and allow functional movement of that major joint: the rotator cuff as dynamic stabilizer, as well as the capsule, labrum complex, other connective tissue elements and glenohumeral ligaments as static stabilizers[15-17].

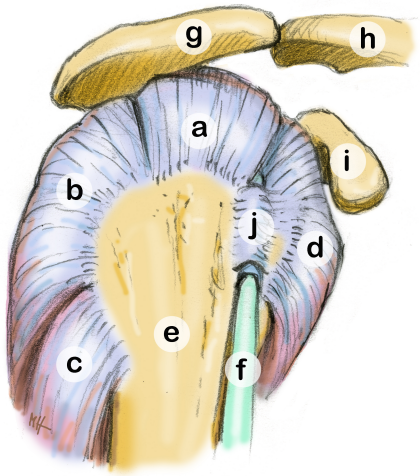


*Figure 2.1 (© M. Haab): Lateral view of the rotator cuff (**a-d**), **a** supraspinatus tendon; **b** infraspinatus tendon; **c** teres minor tendon; **d** subscapularis tendon; **e** proximal humerus; **f** biceps tendon with biceps tendon sheath (**j**); **g** acromion; **h** clavicle; **i** processus coracoideus*

The rotator cuff consists of four shoulder muscles: The musculus supraspinatus which initiates abduction, the musculus subscapularis as main internal rotator, the musculus infraspinatus and teres minor as external rotators[18,19]. All the rotator cuff muscles work as force couples. For compressing the humeral head into the glenoid joint, the supraspinatus muscle works with the deltoid as the coronal force couple. The axial force couple consists of the subscapularis and the infraspinatus muscles. These two muscles work for the compressive joint reaction in the axial plane[19]. Next to holding the humeral head into the glenoid concavity, an other priciple function of the rotator cuff is the

generation of the torque needed for the rotation of the humerus[16,20]. See Figure 2.1 for anatomical illustration of human rotator cuff.

2.2 Rotator cuff tears

Rotator cuff tears are the most common soft tissue injuries in shoulders[3], rendering them to the main etiology for shoulder pain[1,2]. Rotator cuff disease includes the disruption of one or multiple musculotendineous junctions of the glenohumeral joint. The damage of the tendon tissue affects the biomechanical properties of the shoulder. Tears in the tendon of the infraspinatus and teres minor muscles result in weakness of active external rotation with increasing internal rotation. In case of massive rotator cuff disease the tendon of the subscapularis muscle can be involved. This would lead to an increased passive external rotation caused by a weakness in active internal rotation[21-23]. Weakness in arm abduction is variable, depending on the extent of abnormality. Next to the amount of damaged tendons, the depth of the defect is decisive. Beside partial-thickness tears, also full-thickness tears can happen. But even in massive rotator cuff tears, a compensation by the deltoid and other accessory muscles can take place[18].
There are multiple complications, which can excerbate the disease. If motion is applied on the injured tendons, it is possible that the tear size increases. Furthermore, torn tendon fibres are not able to participate in load sharing. The remaining intact tendon tissue would then need to stabilize the entire load of the shoulder. This can lead to tear propagation, especially if that remaining tissue is of poor quality[24,25]. Another complication is tendon retraction following tears. On the one hand, that could have an impact on the subscapular nerve, on the other hand muscle atrophy and fatty infiltration of the supraspinatus and infraspinatus muscles can occur[26,27]. A possible dramatic consequence of the progression of rotator cuff tear is a superior subluxation of the humeral head resulting in a dysfunctional shoulder[18,19].

Up to 70% of all the patients visiting the physician because of shoulder pain are diagnosed with rotator cuff disease[1,2]. There is a much higher prevalence for elder people. While the prevalence for people in their 50s is only 10.7%, the percentage of older patients showing tendon tear issues increase noticeably: 15.2% in the 60s, 26.5% in the 70s and 36.6% over 80 years[1,3,4]. Several studies verified that rotator cuff tears are multifactorial. Risk factors include patient age, arm dominance and trauma[3,28]. Additionally, heavy lifting or repetitive movements especially over the shoulder level

could be a trigger[1]. Depending on the individual pathology, rotator cuff tears can lead to an acute, chronic or acute-on-chronic disease.

An acute etiology is mostly found in younger patients[29]. These patients commonly describe a traumatic case history. Falling onto the shoulder or lifting up a heavy item can cause an acute onset. An acute rupture leads to dramatically increasing pain and rapid loss of function[30].

In most of the cases, however, rotator cuff tears present as a chronic degenerative disease, predominantly in the elderly population[4,13,30,31]. Repetitive overhead activities, for example seen in athletes or laborers, can also cause chronic tendon damage. Clinically a continous decrease of shoulder function and strength takes place. Some of these patients describe a triggering incident, which leads to dramatic worsening of the chronic injury. These cases are defined as acute-on-chronic diseases[30].

Bishay and Gallo described the kind of pain caused by a rotator cuff disease „as a dull, aching pain". Pain increases during night and overhead activities[18]. Next to the pain itself, patients suffer from stiffness or weakness of the shoulder muscles. That can lead to massive disability to carry out daily activities or work[1].

Several studies validated the after effects of rotator cuff disease with or without surgical repair. Untreated rotator cuff tears can lead to associated alterations or injuries of the tendons and surrounding tissue. That includes for example the risk of complete rotator cuff ruptures, followed by lesions and inflammation of the biceps tendon and risk of complete biceps tearing leading to loss of function[5,6]. Furthermore a detachment between the supraspinatus and the infraspinatus muscles is possible[32]. Coleman and Fealy established a chronic rotator cuff disease model in sheep. They found out that the ealier the tendon repair, the faster the recovery time of muscle function and tendon elasticity. The two researchers set a theory about a „point of no return" in rotator cuff injury, after which the elasticity of the muscle-tendon-unit does not return to initial flexibility. That fact would make a more delayed tendon repair useless[33].

Torn tendons with changed structure and composition have suboptimal healing potential[5]. There is a clear correlation between tendon healing, postoperative strength and the clinical score called „Constant Score". The better the healing, the more strength and the better the Constant Score. Another factor influencing the healing is the patients age and the size of the tear. The older the patients and the bigger the tear size, the lower is the chance of healing. Franceschi, Ruzzini and Longo et al. found no association

between tendon healing and gender, duration of symptoms before surgery or previous treament with injections[34].

2.3 Tendon healing and complications

The healing process of ruptured tendon tissue includes three overlapping stages: Inflammation/ hemostasis, proliferation/ fibroplasia and remodeling/ maturation. The phase of inflammation starts directly after injury and lasts for about seven days. Hematoma formation and neovascularisation for cell recruitment and infiltration takes place[17,35]. In that phase mechanical stretching should be avoided[36]. 3-7 days after injury the proliferative phase begins and continues for several weeks. Within the following week, a disorganized matrix of granulation tissue is present. Collagen syntheses and conversion of collagen types occur[17,35]. Cyclic mechanical stretching during that period may have a positive influence on the tendon healing progress by enhancing cell proliferation, differentation and matrix formation[37]. The third and last phase is remodeling/ maturation, which happens over the course of weeks to months to one year after injury. Reorganization of collagen occurs. Macroscopally, the scar tissue turns from red to pinkish and translucent[35,38]. These healing processes are managed by two different mechanism: the intrinsic and the extrinsic pathway. The intrinsic healing includes proliferation of fibroblasts from the epitenon and endotenon, cellular migration to the side of lesion to form a new matrix. The extrinsic way involves sending inflammatory cells and fibroblasts from the surrounding tissue[39].

Another complication in the tendon healing procedure is an inadequate inflammatory reaction. As controlled inflammation is a necessary step within the healing process, persistent inflammation has negative effects on the healing. The main consequence is the excessive production of fibrotic tissue. That leads to adhesions which further limit function of the shoulder joint. Adhesions between the tendon and the tendon sheath inhibit the natural gliding and movement of the tendon in the sheath. Furthermore, fibrotic scar tissue can end in degenerative healing with the risk of rerupture[40-42].
As described, the process of tendon healing can last for up to one year. Several characteristics of tendon tissue biology and biomechanic are tied to that poor healing profile[35]. Especially in the shoulder, the failure of tendon healing is a common problem. Reasons include the lack of an inclusive vascular network and the low metabolism of the cells, leading to a poor intrinsic healing pathway. This results in little regenerative

potential. Tendon regeneration takes place by developing a poor, fibrous scar-like tissue[43,44]. The structure and composition of the collagen in that tissue is less organized than in healthy tendon tissue[45,46]. This results in the high risk of a retear in that weak and prone tissue, especially as a consequence of overuse[43,47]. Also the biomechanical characteristics are affected by the tissue transformation. The tensile mechanical properties may improve towards normal levels, but will never completely regain structural, functional and compositional properties of healthy tendon tissue[35,38,48]. Clinically, that results in reduction of mobility and an increase in pain and morbidity[49].

The outcome of the tendon healing process is greatly affected by the mechanical environment post surgery[50]. Loading influences the tendon remodeling, which triggers structural, biomechanical and mechanical changes. During the early healing phase the level of activity needs to be chosen carefully. The level ranges from disuse to overuse. The goal is to restore normal strength and range of motion without putting the healing area at risk[35]. Several investigators had proven that a complete immobilization of the operated extremity results in decreased mechanical properties and deter functional recovery. Controlled loading is optimal. Excessive weight bearing is absolutely disadvantageous to the injured tendon. This can lead to impaired healing, injury, adhesion formating and failure of repair[50,51]. For protection against overload it can be helpful to use a sling[52].

2.4 Rotator cuff repair

Rotator cuff repair can be achieved by a variety of possible treatment options. The main goals of an ideal rotator cuff repair are restoring biomechanical properties, decreasing pain, improving funcional ability through achieving a strong fixiation of the repair to allow a more aggressive and effective rehabilitation program[53,54]. To choose the exact kind of treatment, several facts need to be combined: symptoms, signs, investigated findings, previous treatment, a knowledge of the exact pathology causing the problems and evidence about the likely outcome of the surgery. In the field of rotator cuff disease, there is a wide range of examination findings, tear size, co-morbidities, the type and duration of previous treatment, as well as evidence about the outcome. That is why a decision about the optimal treatment must be made for each patient individually[2]. Several studies showed a better tendon healing potential in repaired rotator cuff tears after surgical repair[55].

2.4.1 Conservative treatment

The treatment options for rotator cuff disease are correlated to the severity of the disease. The conservative treatment is the most non-invasive option. A nonoperative management is indicated for largely intact rotator cuff force couples with mainly functional related symptoms[56]. That program can include pharmacology (non-steroidal anti-inflammatory drugs), physical therapy (for example strengthening of the deltoid and persiscapular musculature), injection therapy (steroids, sodium hyaluronate) and exercise rehabilitation[16,29,56,57]. It is possible to manage patients with moderately symptomatic massive rotator cuff tear with a nonoperative treatment, but the risk of negative effects is notable. A non surgically treated massive reparable tear can progress to an irreparable tear within four years. This worsening can be caused by fatty infiltration of the muscle, increasing of tear size and progressing glenohumeral osteroarthritis[58,59].

2.4.2 Massive irreparable tears

If a nonoperatively management failed or the disease severity excludes conservative treatment, surgery is required. Depending on the exact pathology and clinical findings, a choice must be made from a wide range of repair options. The worst case scenario is an irreparable rotator cuff tear. The goal is not to repair the tendon but to improve the shoulder function, range of motion, strength and relief pain[60-63]. For example, in case of irreparable painfull full-thickness tears in elderly patients, there is the possibility of debridement and biceps tenotomy[62-65]. The latter is recommended since after massive rotator cuff tears, lesions in the long head of biceps tendon are seen relatively often and cause notable pain[66]. Reducing the pain is one of the main goals which can be achieved[62,63,66]. Restoring of functionality is also possible, because pain caused by mechanical impingement will be reduced[65]. Another surgical treatment for massive rotator cuff diseases is the tendon transfer, for example the latissimus dorsi transfer. The main indications for that surgery is a massive irreparable rotator cuff tear with poor quality of tendon tissue. The goal is to improve the shoulder function, range of motion and strength and the relief of pain. Several studies proved that there is a realistic chance to achieve all these goals. Although no „normal“ shoulder function or complete pain relief can be achieved, that treatment is often the only option for younger and active

patients to restore shoulder function and strength as well as decreasing pain[60,64]. The latissimus dorsi transfer is mostly done in young and active patients who show only minimal glenohumeral arthritis in combination with severe loss of function. The surgery is done to restore anterior and posterior biomechnical force couples of the shoulder joint[60].

2.4.3 Reparable tendon tears

Many cases are presented where a surgical repair of the torn tendon itself is possible. The biomechanical goal is to create a normal insertional anatomy of the tendon footprint. To achieve an optimal healing environment, there should be low tension on the repair during the healing period[67]. The quality of the tendon tissue and the shape of the ruptured tendon (crescent-shaped, U-shaped, L-shaped and retracted tears) is deciding for the outcome[67,68]. The repair must be strong enough to withstand physiologic loads until the tendon tissue is healed. The gap size must be minimized and the damaged tendon stabilized without creating tissue strangulation and necrosis. Finally pain relief and restoration of function should be achieved[67].
Different varieties of suturing techniques are described. Depending on the exact pathology, one can choose the way of reattaching the tendon to the bone, the suture pattern itself and also the suture material. The fixation of the tendon to the humeral head can be achieved either by a single or a doube row repair. That means a single or a double row of anchors is pinned into the bone. For a single row repair, different matching types of patterns are available: Simple sutures, mattress configuration, modified Mason-Allen stitch, rip stop and a massive cuff stitch. The modified Mason-Allen Stitch is a combination of a horizontal mattress and a vertical single suture[67].

The double row repair includes a second row of bone anchors and can be achieved with the following types of fixation techniques: Classic double-row and the transosseus equivalent (knotted or knotless), which is also called suture bridge technique[67,69].

Evaluating the outcome of multiple studies using the single row techniques, the modified Mason-Allen stitch and the massive cuff stitch showed the highest ultimate tensile load compared to the simple or the mattress stitch[2,67,70]. The Mason-Allen stitch came up as the strongest single row suturing technique without causing necrosis and showing a good biological tolerance[52,67]. There was no significant difference in cyclic

elongation, peak-to-peak displacement, mean load to failure and stiffness among single suture techniques[67]. The simple and mattress stitch mainly failed by pulling out the suture through the tendon tissue[67]. That effect is called cheese-wiring[71].
Comparing the single and double row suturing techniques, a double row repair shows a higher ultimate tensile load and contact pressure[67] by increasing the number of points of fixation. Decreasing the load each anchor must resist leads to reduced stress at each suture-cuff contact point[69]. Most investigators found no significant clinical improvement by using a double row instead of a single row repair[34,67]. In contrast to that, other researchers found a lower retear rate for rotator cuff tears treated with a double row repair[53,72,73]. The reason behind this differing results is not clear yet.

2.4.4 Surgical repair suture material

Next to the suturing techniques, the suture material is decicive regarding the biomechanical and clinical outcome. An ideal suture material should be strong enough to withstand applied force, especially during healing period[74]. While guaranteeing a stable repair, the suture should not be too stiff. Stiffness can cause soft tissue damaged and repair failure by cutting through the tissue[75]. Furthermore, viscoelastic properties of the material are a critical factor[76]. To prevent gap formation the suture needs to have low initial extension, creep and relaxed elongation. Gap formation between tendon ends over 3mm is defined as a failed repair[76]. Other important characteristics are good handling, knot and loop holding security, resistance to abrasion, ability for knots to slide smoothly, adequate knot dimensions and suture thickness[68,74,76-78].

Nowadays five suture materials are mainly used in rotator cuff repair surgeries: MagnumWire (ArthroCare, Austin, TX), Ethibond (Ethicon, Somerville, NJ), Fiberwire (Arthrex, Naples, FL), Orthocord (DePuy, Warsaw, IN) and Force Fiber (Tornier, Bloomington, MN)[76]. Several studies compared the biomechanical properties of these sutures, where Fibrewire mainly showed superior results. Fibrewire has a multistranded long-chain ultra- high–molecular weight polyethylene core and is coated by a braided PET polyester-ultrahigh-molecular-weight polyethylene jacket[78]. As a high strength suture material, Fibrewire was sufficiently strong and had better results in knot and loop security than other commonly used high-strength polyethylene suture materials[78,79]. Furthermore, Fiberwire shows the smallest creep during creep testing, lowest initial extension and smallest peak-to-peak displacement[76]. Even damaged Fibrewire suture

material achieved good biomechanical results[78]. Another characteristic of the Fibrewire suture material is higher stiffness compared with the other sutures[76]. The latter may cause the cheese-wiring effect by cutting through the tendon tissue[71]. Fiberwire also shows a tendency to fail by slippage at a low load, thereby needing backup suturing[80].

2.4.5 Surgical approaches

Possible approaches for the surgery are the following: arthroscopic, mini-open or open[18]. Nowadays the arthroscopic technique is the standard of care for rotator cuff repair[67]. Studies showed comparable results for arthroscopic and open repair for tears less than 3cm. Massive tears greater than 3cm achieved better results by repair with open approach[81]. The arthroscopic approach resulted in a much smaller incisicion, less soft-tissue dissection and less post operative pain[34,81]. However, some suturing techniques are rarely used via arthroscopic approach, for example the modified Mason-Allen stitch. Multiple transtendinous passes are more difficult to make with an arthroscopic approach[67].

2.5 Current problems with repair

One of the main complications of rotator cuff surgeries is the retearing. Several studies showed a failure rate of 21% up to 95% in humans, depending on the exact study plan[9,10]. Other investigators also reviewed a retear frequency of about 15% to 95%, which could clearly be noted on postoperative imaging[81-84]. The mechanism causing a retear is the pullout of intact sutures through the repaired tendon or cheese-wiring[71,85,86]. As the suture-tendon interface is a weak point, the tendon quality is crucial for healing success[86,87]. Other mechanisms of repair failure can be bone tunnel or bone anchor related, for example bone tunnel breakage, suture cut through the bone tunnel, anchor instability or pullout[88,89,90]. Shoulder research described the use of bone tunnels to be potentially advantageous compared to bone anchor techniques[91]. Another important aspect is the preoperative tear size. There is a noticeably higher risk of retear in full thickness tears compared to a partial thickness injury[9,10,92]. Furthermore researchers also found a directly correlation between retear rate and age. Advancing age is a dominant factor because of its association with fatty degeneration, decreased resilience of tissue trauma, poorer tissue perfusion and depleted stores of growth factors pivotal for proper tendon healing[93-97]. In a study of Rashid and Cooper, they investigated an overall rate of failure of 43% one year postoperatively. The more severe the tear size and the older the

patients, the higher the failure rate. Small tears found in patients with a mean age of 59 years showed a retear rate of 34%, while surgery in massive tears failed in 73% of the cases with a mean patient age of 66 years[8]. Furthermore, the vascularization is deciding for the healing chance[98]. The microvascularization of tendon is oriented parallel to tendon fibers and progresses from medial to lateral. Based on that anatomical knowledge the stitches should respect the vascularization. That's why the suturing technique is an other factor influencing the outcome[7]. A suture row constructed transversally to the direction of the blood vessels will enlarge the risk of ischemia and retear[98,99]. Other factors for a tendon retear is muscle atrophy, increased scarring, decreased range of motion[100] and forces transmitted through the repair which influence the strength of the repaired tendon in the rehabilitation process[101]. Next to the already mentioned risk factors, an inappopriate postoperative rehabilitation management is also important[10,93,102-104]. Nevertheless, there are a few factors for which no correlation to healing rate could be found: completeness of repair based on the extent of footprint coverage[86], etiology of the rotator cuff tear, side of the repair, hand dominance, time between first symptoms and surgery, shape of the acromion, exact location of the tear, biceps tenodesis and the kind of post operative immobilization[94,95].

There is a correlation between tendon healing and clinical outcome. Different investigators verified an increased shoulder function and muscle strength after a repair with decreased tear size, even when the healing is incomplete[105]. As mechanical defects of the rotator cuff cause muscle weakness and functional impairment of shoulder, a healed tendon is advantageous for the patient[93]. To avoid retear, a proper postoperative protection of the repair is important. Most of the retears occur between week 6 and 26 post surgery, during which the rehabilitation program and the allowed activity needs to be controlled[7,106].

2.6 Sheep model

Worldwide the sheep model is a common animal model for shoulder repair and different suturing techniques[11,107]. Sheep are a convenient large animal for research because of availability, easy handling and housing, animal costs and the acceptance of the society as a research animal in comparison to dogs[108]. The rotator cuff tear in humans mostly happens in the tendon of the suprapinatus muscle[93], which has a similar size compared to the sheep's infraspinatus muscle and tendon[52,109], see Figure 2.2 and 2.3 for

anatomical illustrations. Furthermore the geometry and mechanical properties of the sheep's infraspinatus and the humans supraspinatus tendon are relatively similar. That is why the sheep model serves as a good approximation for human anatomy in rotator cuff repair[101].

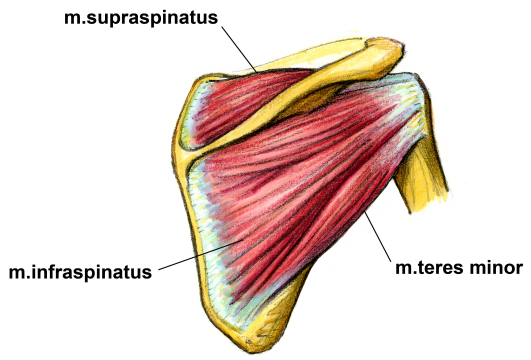


Figure 2.2: Human shoulder (© M. Haab)

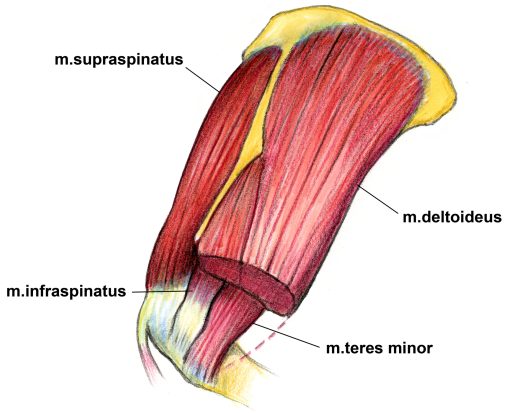


Figure 2.3: Ovine shoulder (© M. Haab)

2.7 Dynacord suture material

The new suture material called Dynacord™ (DePuy Synthes Mitek Sports Medicine, Raynham MA) is a suture that has been designed to minimize suture laxity during the healing period. If a minimum amount of tension is not applied to the suture, an inner core of salt-impregnated silicone expands radially and the suture shortens in length until tension is restored. This is designed to accomodate to sudden movement that patients may make during the healing period. Except for being oversized in diameter, this suture meets the United States Pharmacopeia (USP) requirements for #2 suture. It comprises inner and outer sheaths manufactured primarily from fibers of ultra-high molecular weight polyethylene (UHMWPE) and polyester Poly (ethylene terephthalate). A round needle (MO-7 Taper Point Half Circle Needle) is mounted at one end.

2.8 Previous studies

Prof. Dr. Brigitte von Rechenberg and the team of the Musculoskeletal Research Unit already run 3 initial pilot studies for testing the behaviour of Dynacord suture material in a sheep model. From Pilot 1 to Pilot 3 surgical and assessment procedure was evaluated and modified. Repairing back a full cut of infraspinatus tendon was tested, as well as a partial cut. One study plan included a second, more proximal relief cut of the tendon. Moreover, positioning and amount of the markers was varied. For ex-vivo evaluation, macroscopic evaluation and measuring was done using markers stitched into the tendon (wire suture). Next to that, assessability of radiographic measurement and histological analysis was tested. The partial cut of the infraspinatus tendon close to its insertion at the humeral greater tubercle without an additional relief cut at the musculotendineous junction proved best and was accepted as a model by the Federal Drug Administration (FDA) in the USA.

3 Material and Methods

3.1 Structure of study

For the study 24 adult female sheep were divided into four groups. Each group contained six animals. The animals were diveded into Treatment with DYNACORD™ (test item = TI) and Fibrewire (reference item = RI). Half of the animals were examined 6 weeks after the surgery, the other half 13 weeks after surgery *(see Table 3.1)*. Every sheep was operated on the right shoulder. The other shoulder was intact. As the correct TI was not delivered when needed, a total randomization was not possible. The randomization was applied to the 13-week groups only. See Appendix 8.1 for treatment allocation.

Treatment	# of animals	Survival	Code
TI	6 sheep	6 weeks	6wTI
TI	6 sheep	13 weeks	13wTI
RI	6 sheep	6 weeks	6wRI
RI	6 sheep	13 weeks	13wRI

Table 3.1: Animal Distribution

3.1.1 Animal experiment

All animal experiments were conducted at the Musculoskeletal Research Unit (MSRU), Winterthurerstrasse 260, 8057 Zurich, Switzerland according to the Swiss laws of animal protection and welfare (Tierschutzverordnung / Tierschutzgesetz (TSchG 455)). The animal experiment was authorized by the cantonal ethical committee under the animal permission number ZH039/17.

3.1.2 Experimental procedure

The efficacy of TI compared to RI was evaluated using the modified version of a previously developed rotator cuff tear model (Gerber et al., 1999 and MSRU Study MSRU0058) and tested in the pilot studies 1-3. Experiences and results of these previous studies led to the current study model. On each animal, only a uni-lateral treatment of the right shoulder was performed. The caudal half of the infraspinatus tendon was transected at its attachment to the greater tubercle of humerus and repaired back with two series of baseball stitches using TI or RI. The sutures were brought

through bone tunnels in the tuberosity and tied tightly around a button plate fixture, leaving a 5mm gap between the tendon and the bone. Additional marking points, steel wire loops and screws, were implemented for taking distance measurements of the tendon during surgery and sacrifice days. A button plate was chosen over suture anchors for re-attaching the tendon to bone because the goal of this study was to evaluate the healing response of the tendon/bone interface with two different suture materials. The suture/tendon and tendon/bone interfaces are the same regardless of the hardware used at the boney insertion. Button plates have been employed in this animal model in previously published studies (Gerber et al., 1999 and Baleani et al., 2003).
See Figure 3.1 for schematic representation of the repair.

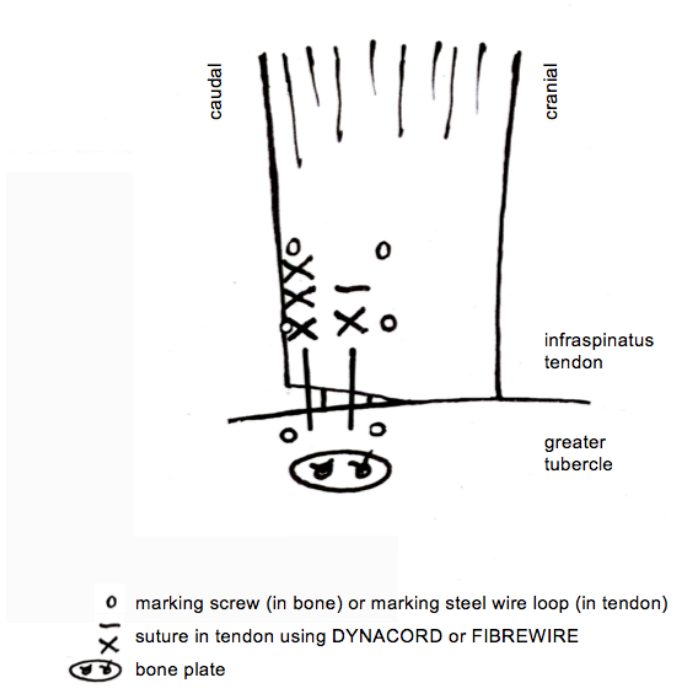


Figure 3.1 (© M. Haab): Schematic representation of ovine infraspinatus repair

Animals were placed in suspension systems for a period of two weeks post-operatively to avoid overload of the tendon by getting up and laying down. Endpoints included measuring distances between the inserted markers and comparing them to the original measurements, biomechanical strength of the healed portion of the tendon and macroscopic analysis of the tendon. The main goal of this study was to compare the biomechanical strength of the healed infraspinatus tendons treated with the RI or the TI.

3.1.3 Animals

The experimental sheep are female Swiss Alpine sheep, which are hosted on a farm and are subjected to a firm prophylactic health management protocol. They receive vaccination with Ovilis® Heptavac P ad us vet (2ml/sheep s.c., Veterinaria AG Zürich, Switzerland) against pasteurella and clostridia. As a prevention against ecto- and endoparasites the sheep are treated with Doramectin (0,2mg/kg BW s.c., Dectomax®, Pfizer AG, Zürich). Every six to eight weeks the claws are cut. Twice a year (every spring and autum) the sheep get clipped by a professional shearer. All sheep have daily access to a pasture. For the study sheep with an age of about two years were chosen, with an average bodyweight of 53.28 kg (45-60kg) at the day of arrival at Strickhof. The animals were acclimatized for at least 7 days under test conditions. The health was examined at the day of arrival and espacially the right shoulder was checked for some abnormalities. Every animal got a blood and chemistry screen. Only sheep without any visible signs of illness and normal blood results were used for the study. Every sheep received a personalized eartag and a subcutaneos transponder for secure identification.

3.1.4 Suture material

The test item was the DYNACORD® suture size 2, blue coloured with the Lot ♯L458948. The test item was supplied by the sponsor, sterile packed and „ready-to-use“.

The reference item was the Fibrewire® suture, size 2, blue coloured with Lot ♯13179. The reference item was supplied by Arthrex (Naples, FL, USA), sterile packed and „ready-to-use“.

Both items were stored dry and at room temperature.

3.2 Preparation

At least seven days before surgery, the animals were selected at the farm and transported to the animal hospital. They got a clinical examination as general health check and the bodyweight was determined. Within the week before the surgery the animals were able to adapt to the test conditions (stable, water, food, handling). A blood examination was made a few days before surgery to check the health status for the forthcoming anesthesia. Twice a day sheep were observed by a veterinarian of the MSRU. 24 hours before surgery sheep were fastened. Access to water was unlimited.

3.3 Surgery

3.3.1 Preparation for surgery

At surgery day the sheep received a clinical examination before premedication. In case of any abnormalities a reserve sheep was available. Half an hour after the premedication the sheep were transported to the surgery theater and a venous catheter was placed. Via that catheter the prophylactic antibiotic and analgetic medication was given. Afterwards the right shoulder was shaved. Thereafter, the animals were examined by the anesthesist. Following sedation anesthesia was induced, an endotracheal tubus was placed and the sheep was positioned in left lateral recumbence on the surgery table. Details about seation and anesthesia are described below (see 3.3.2. Anesthesia). The right shoulder was cleaned and desinfected. Furthermore the claws were cut, an eartag with individual animal number and a transponder for identification were set. In addition to that, an arterial catheter was set in an auricular artery by the anesthesist.

3.3.2 Anesthesia

Sedation of the sheep was achieved with xylazine (0.1 mg/kg BW i.m., Xylazin Streuli ad us. vet., Streuli Pharma AG, Uznach, Schweiz). Analgesia was provided through the injection of buprenorphine (0.01 mg/kg BW i.m., Temgesic®, Reckitt Benckiser AG, Wallisellen, Schweiz). After placing the jugular catheter the animals received benzylpenicillin (30.000 IU/kg BW, i.v., Penicillin natrium Streuli ad us vet, Streuli Pharma AG, Uznach, Schweiz) and gentamycin (4mg/kg BW, i.v., Vetagent® ad us. vet., MSD Animal Health GmbH, Luzern, Schweiz) as prophylactic antibiotic therapy. As antiinflammatory and analgetic therapy carprofen (4mg/kg BW, i.v., Rimadyl®, Zoetis Schweiz GmbH, Zürich) was injected. Additionally, every animal received tetanus serum (3 ml/ sheep, s.c., Tetanus Serum Intervet, MSD Animal Health GmbH, Luzern) for prophylaxis.

Anesthesia was then induced with ketaminhydrochloride (3 mg/kg BW i.v., Ketanarkon 100 ad us. vet., Streuli Pharma AG, Uznach, Schweiz) in combination with midazolam (0.1 mg/kg BW i.v., Midazolam Sintetica, Sintetica S.A., Mendrisio, Schweiz) and propofol (0.3 - 1.3 mg/kg BW i.v. or more as needed, Propofol 1% MCT Fresenius, Fresenius Kabi (Schweiz) AG, Oberdorf, Schweiz). For a balanced anesthesia, inhalation anesthesia with isoflurane (Attane™, Isoflurane ad us. vet., Provet AG, Lyssach, Schweiz) in oxygen and a constant rate infusion of propofol was administered.

All animals were monitored for cardiovascular problems, which included electrocardiogramm, heart rate, pulse rate and directly measured systolic, mean and diastolic arterial blood pressure via an arterial catheter.

3.3.3 Surgical technique

While laying in left lateral recumbence *(see Figure 3.3 A)*, a lateral curved incision over the shoulder joint was made. the fascia was incised and infraspinatus tendon exposed *(see Figure 3.3 B)*.

Then measurements of the tendon width at the bone insertion and the muscle insertion was taken and recorded. The caudal half of the tendon was then transected at its attachment to the tuberosity *(see Figure 3.3 C)* using an 11 blade scalpel. The length of the transection was 50% +/- 10% of the total width of the infraspinatus tendon at the tuberosity. The spontaneous gap size was measured immediately after cutting. Afterwards four drill holes were made into the bone at the insertion of the original tendon towards the anterior aspect of the greater tubercle for passing shuttle sutures through the bone tunnel *(see Figure 3.3 D)*. For each suture a deep and more superficial bone tunnel was made, such that the upper and lower suture of each Mason-Allen suture could be inserted into separate tunnels and tightened with each other over the button plate. The partial cut was then repaired with two series of baseball stitches (modified Mason-Allen stitches) using the test or the reference item *(see Figure 3.2 and 3.3 E)*.

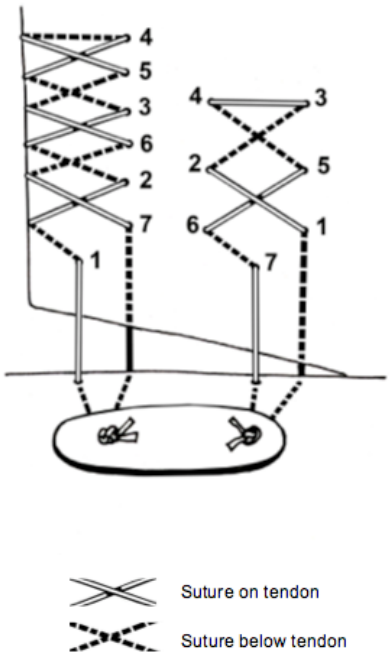


Figure 3.2 (© M. Haab): Schematic representation of the stitching pattern of both suture rows

There was a distance of approximately 10mm +/- 2mm between each baseball stitch. Because of the different appearance of the test and reference item, it was not possible to blind the surgeons. There was another measurement of the gap size after tendon suturing but before suture passing and tightening to evaluate the gap size after tendon manipulation. A maximum gap of 5 +/- 1 mm at the caudal margin of the cut tendon was created by interposing the muzzle of a needle holder in between the tendon and the bone. Then suture material of the test or reference item was brought through bone tunnels in the tuberosity by using shuttle sutures. The sutures were tied by passing them through the holes of the butto plate fixture cranially or caudally while the needle driver still opend the gap *(see Figure 3.3 F)*. A relief cut more proximal of the tendon, as done in one of the previous pilot studies, was not performed.

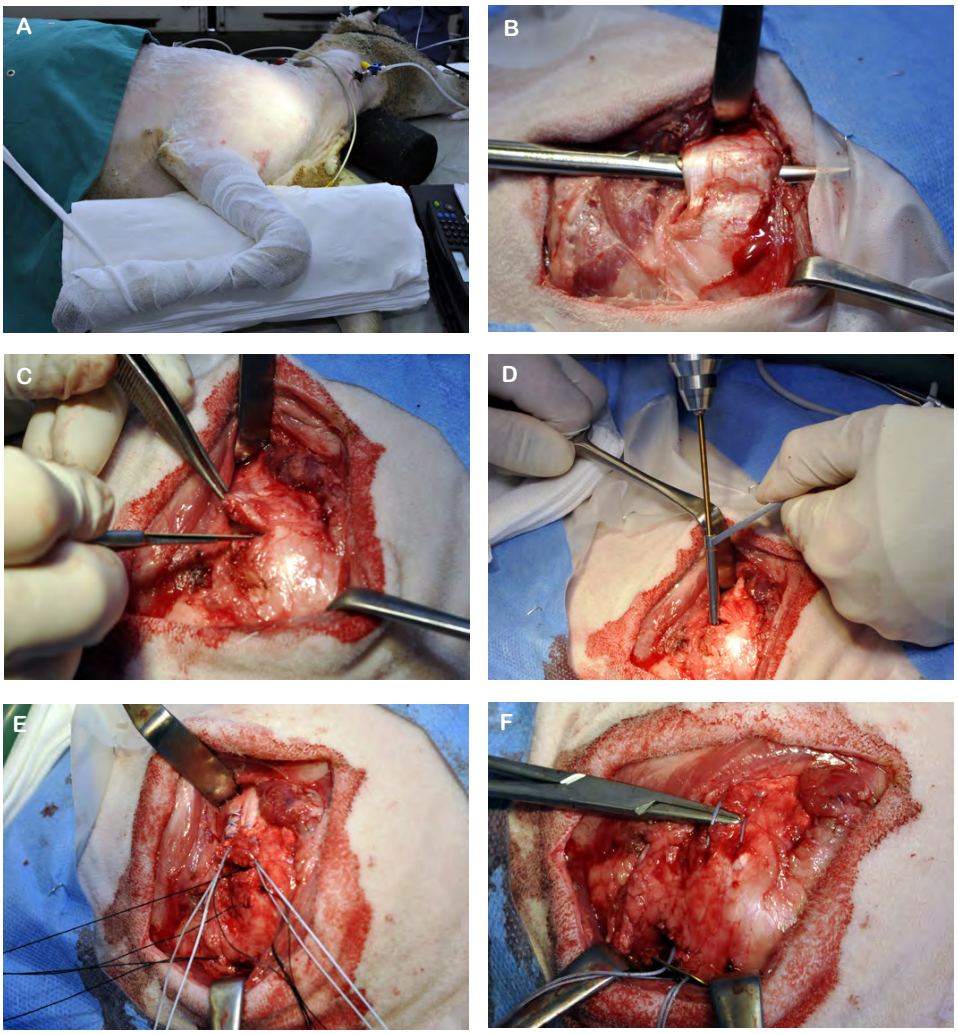


Figure 3.3: Representative picture showing sheep positioning (A), exposed infraspinatus tendon (B), partial tendon transection (C), drill hole creation (D), baseball stitchs and shuttle sutures (E) and the 5 mm gap created by the needle driver (F).

After the tendon repair the surgery was finalized using additional marking stitches (steel wire loops; Ethicon 3/0 monofil suture non-resorbable) and 2.0 mm screws (Synthes 401.360.97 2.0 mm Titanium Cortex Screws, self-tapping, with StarDrive recess) were placed as follows:

One pair of steel wire loops was placed at the level of the musculotendineous junction and one pair of steel wire loops was placed between the first and second stitch of the Mason-Allen suture. The caudal stitch of the pair was placed at the edge of the tendon, the more cranial stitch was placed at the same height at the longitudinal axis to the 50% partial cut of the tendon. An attempt was made to have a symmetrical rectangle. One screw was inserted ca. 2 mm caudally, one cranially into the bone at the insertion of the entire tendon without entering the bone tunnels.

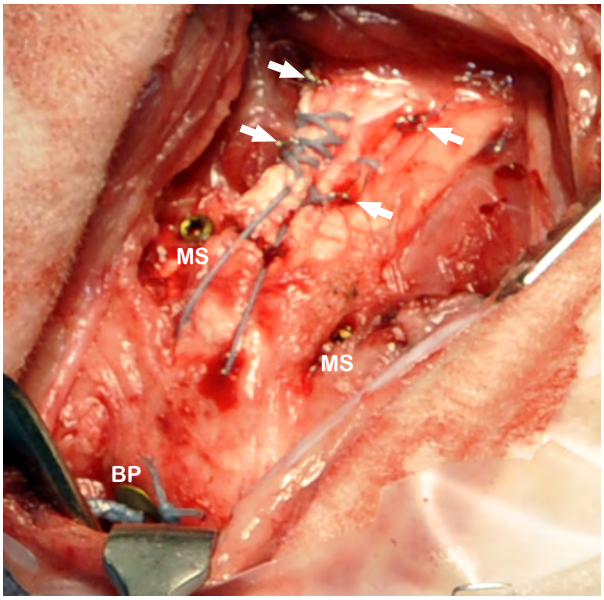


*Figure 3.4: Representative picture showing the suture repair: **BP** button plate; **MS** marking screws; **white arrows** steel loops*

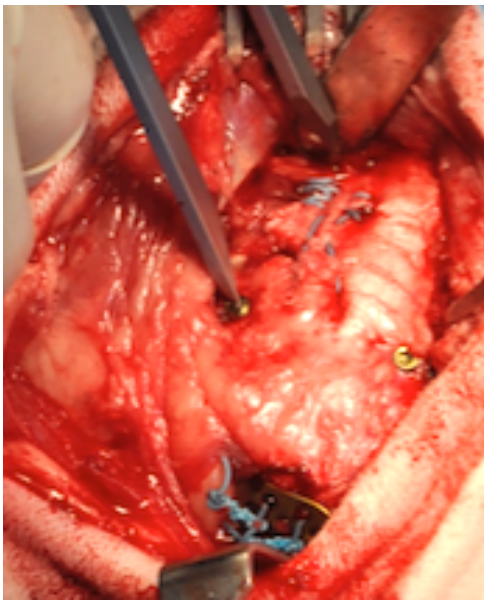


Figure 3.5: Representative picture showing distance measuring by custom Vernier Caliper

The screws and steel wire loops were then used to measure several distances inbetween these marking points. The measurements were taken by a custom made Vernier caliper which was provided by the sponsor *(see Figure 3.5)* and noted in a measurement sheet *(Appendix 8.2)*.

In the pilot study (study number MSRU0058), it was found that X-ray measurements were insufficiently accurate, due to the wires and screws not all being in the same plane. Additionally, it is impossible to standardize the position of sheep in vivo with respect to the shoulder after sacrifice. Therefore, measurements in this study were taken with the caliper at the time of implantation during surgery and at sacrifice. This was done to

provide an adequate understanding of the laxity in the repair during the healing period (Details see 3.5 Evaluation methods).

After measuring the incision was closed in layers and the skin was stapled. The animals were then placed on a stretcher in left lateral recumbence and directly placed into the suspension system. The sheep stayed in the surgery hall until the endotracheal tubus was removed. After that, the animals were transported to the stable and mounted in the suspension system. This partial weight-bearing system permitted standing, turning, and walking within the pen, but prohibited lying down, uncontrolled limb movements and vigorous activities.

While preparation and surgery representative photographs were taken *(see Figure 3.3 to 3.5)*.

3.4 Post-operative treatment and care

Right after the transportation to the stable, the sheep where placed in the suspension box. While still laying on the ground the sheep got access to hay. At the moment they were completely awake and fit, they where mounted in the suspension system by at least two people of the MSRU personnel. By pulling them up with the rope of the suspension system, it is possible to help them standing up without putting some weight on the operated right front leg. The sheep were observed at least 3 times within the first 2 hours after surgery. The MSRU personnel always stayed in the stable until proper standing and eating was observed. In the following hours a veterinarian checked them regularly at least every 4-6 hours for the application of analgetic medication (Buprenorphin, 0.01 mg/kg BW i.m., Temgesic®, Reckitt Benckiser AG, Wallisellen, Schweiz). In the next days all animals were observed at least twice a day through a veterinarian. These checks included the scoring of alertness, posture, appetite, respiration, pain, lameness and especially the operated region (right shoulder) as well. For the right shoulder it was important to evaluate whether exudation, swelling or other abnormalities took place. For pain management carprofen (Rimadyl®, 4mg/kg BW, i.v.) was given for another 4 days after surgery. As a prophylactic antibiotic therapy Penicillin (30'000 IU/kg BW, BID, i.v.) and Gentamycin (4 mg/kg BW, SID, i.v.) was continued for 4 days postoperatively. After the last application of medication the venous catheter was removed. Three weeks after surgery the skin staples were removed.

Two weeks after surgery the sheep were taken out of the suspension system and were kept in small groups of 2-3 sheep still in small groups. As sheep are really social animals, only in case of severe lameness sheep were excluded from company of their companions.

In case of good health status, sheep were allowed to move to the farm (Staffelegghof) the earliest 3 weeks post surgery, where they were still confined to small pasture. For the transportation a cattle trailer was used. The sheep were always transported in company of their companions. After the transfer to Staffelegg all animals were checked twice daily for abnormal clinical signs. In addition, once per week a veterinarian or a veterinary engineer performed a basic health check of each animal to note abnormalities (for example state of operated front limb, abnormal behavior of any kind, feeding loss, diarrhea, seclusion from the herd / group, injuries, lameness, death, birth, etc.). Over night all the sheep stayed at the stable in small groups, at the day they had access to a small pasture. They had free access to fresh water and were fed with hay ad libitum.

If the sheep had been transported to Staffelegg, they removed a few days before sacrifice day to Strickhof. At the day of arrival the sheep were examined and the actual body weight was detected.

Depending on the sheeps character and on how far they had to be transported on the Tierspital area on the sacrifice day, it was decided whether they need a sedation or not. A venous catheter was then administered to guarantee a safe and rapid euthanasia. At least 40 mL Pentobarbital was then administered intravenously, with the possibility of administering additional 10mL doses if necessary. The death was confirmed by auscultation (absence of heartbeat) by a veterinarian. The operated front limbs were then harvested by cutting the shoulder girdle muscles medial to the scapula.

3.5 Evaluation methods

3.5.1 Macroscopic evaluation

The suture type (test or reference item) was blinded to the person performing the macroscopic evaluation (Prof. Dr. Brigitte von Rechenberg).

The repaired tendon was carefully approached by stepwise dissection of the surrounding tissue. A score sheet *(Appendix 8.3)* was used to provide a standardized macroscopic evaluation and scoring. Basically, the score sheet is composed of three parts:

The first part notes the general impression of the surrounding soft tissues. Signs of inflammation or hematoma are evaluated as well as the extent of fibrosis.

The second part takes a closer look at the tendon and the repair site to evaluate whether the tendon and the sutures are still intact. Also, the visual condition of the tendon and potential tendon affection by the sutures is taken into consideration. The knot security of the sutures is tested and the position of the bone plate assessed. Unexpected lesions including their location and severity are noted.

In the last section, the distances between markers, proximal and distal tendon width will be measured and marked on the measurement sheet *(Appendix 8.2)*.

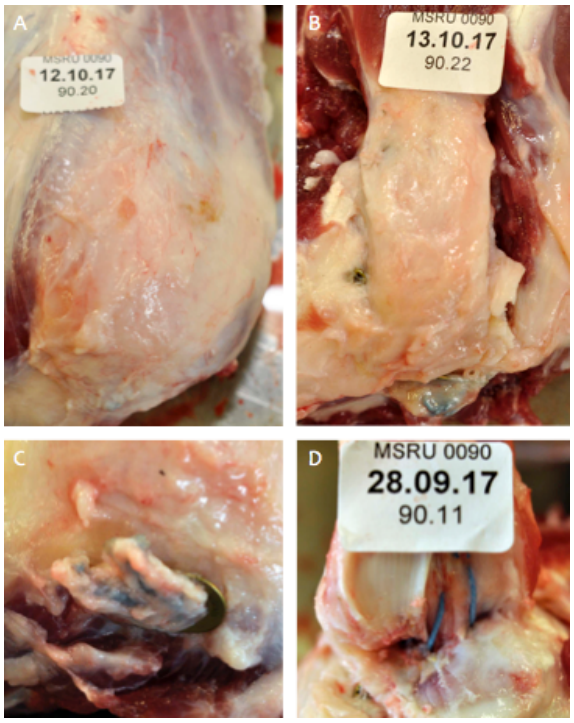


Figure 3.6: Stepwise dissection; Overview shoulder joint (A), Infraspinatus tendon (B), Bone plate (C), Repair site with tendon dissected from the insertion and flipped over (D)

Representative photographs were recorded *(see Figure 3.6)*. Findings that were not covered within the score sheet were noted separately (for example marker loosening or model disintegration, tendon necrosis, seroma, calcinosis, etc.).

After the macroscopic evaluation the samples where prepared for the biomechanical testing by MSRU personnel. For this the infraspinatus muscle was transversally cut

approximately 3-4 cm proximal to the musculotendinous junction and the muscle tissue was laterally and medially removed until the central tendon was visible (*see Fig. 3.6*). The scapulohumeral joint was opened and the proximal humerus was subsequently separated from all other muscles and tendons. Finally, the humerus diaphysis was also freed from all adjacent muscles and cut transversally just proximal to the elbow. In the last step, the still intact (cranial) portion of the tendon was released at the insertion site in order to test the strength of the repair tissue only. Afterwards the humeral head was resected with a band saw in order to prevent impingement with the test machine and the humeral periostium was dissected as well as remaining muscular tissue of the bone and central tendon.

After that preparation the samples where wrapped in saline soaked gauze and placed in an insulated box. The specimens where transported under these conditions to the test facility for biomechanical testing (Institute of Biomechanics at the ETHZ, Prof. Stephen Ferguson's laboratory).

3.5.2 Biomechanical testing

3.5.2.1 Sample Preparation

The suture type (test or reference item) was blinded to the person performing the biomechanical testing.
Arrived at the ETHZ the sample preparation for the testing was completed by Prof. Stephen Ferguson:
The cut end of the humerus was potted into a plastic ring with PMMA (Beracryl D-28, Suter Kunststoffe AG). Holding rings were used to keep the specimen in position during the curing. The specimens were wrapped in saline-soaked gauze to prevent the tissue from drying. The tests were conducted on the Instron ElectroPuls E10000 Linear-Torsion material-testing machine with a custom-made test setup. The tendons were clamped in a custom-made cryoclamp cooled with dry ice.

Prior to biomechanical testing, the sutures strands were cut (by MSRU personnel present at the test location) between the 7-hole plate and the bone. By detaching the sutures, only the healed zone effectively bear weight when traction was applied to the tendon. Representative photographs were taken as well *(see Figure 3.7)*.

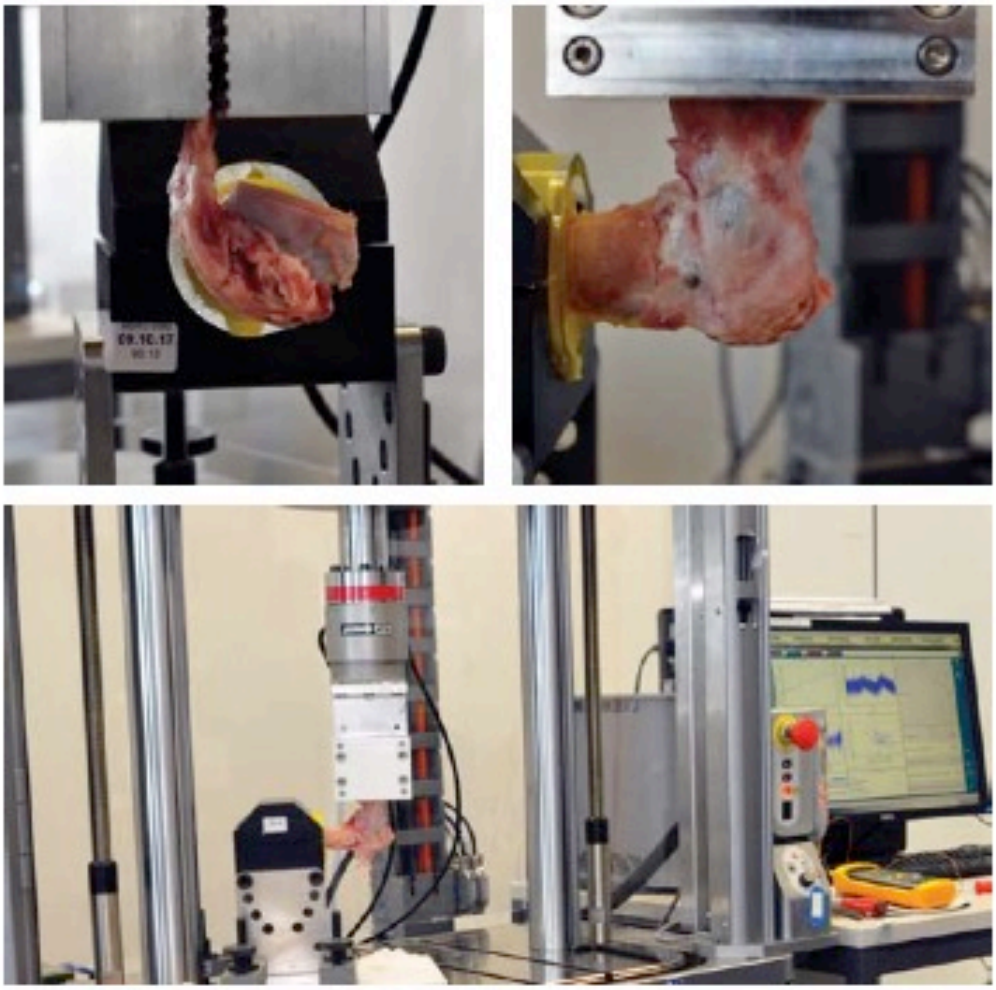


Figure 3.7: Representative pictures showing sample mounting setup onto the Instron machine.

3.5.2.2 Biomechanical testing parameters

The biomechanical test was split into two main steps:

The first step was the non-destructive loading test: First the tension on the specimen was increased with a force-controlled linear ramp of 1 Newton per second (1 N/s) until 20 N were reached. Then the 20 N were held for 120 seconds using force control before starting 10 sinusoidal force-controlled loading cycles between 10 N and 30 N in tension.

Second step was the destructive loading test: After the cyclic non-destructive loading, a linear destructive displacement controlled loading ramp of 1 millimeter per second (1 mm/s) was applied as soon as the specimen fails (tendon-bone interface rupture) the test was stopped manually.

Apparent stiffness, ultimate strength and yield point were calculated from the load-displacement curves.

The apparent stiffness describes how much force is needed to deform the material by a given displacement. The apparent stiffness was evaluated for the non-destructive cyclic

loading by a linear regression of the force-displacement data, where the slope of the regression line represents the apparent stiffness. The first loading cycle was considered as pre-conditioning and was therefore systematically excluded from the stiffness calculation for all 24 specimen. The apparent stiffness was also evaluated during the destructive loading between 5% and 50% of the maximum detected force. Curves from samples 90.04, 90.08, 90.16, 90.18 and 90.22 showed evidence of slippage (tissue-clamp or tissue-internal) during the loading. Therefore, the evaluation of stiffness was performed on a region of the loading curve between two bounding values, which were defined manually to exclude any slip.

The ultimate strength defines the maximum force that the tested specimen could sustain. The ultimate strength was evaluated during the destructive loading by recording the maximum force that occured during loading.

The yield point is reached as soon as the deformation of the specimen becomes irreversible. The yield point was evaluated during the destructive loading by calculating the gradient of the force-displacement data during the loading phase. The yield point was then defined as the point where a gradient drop of 50% is detected. 50% was a chosen criterion based on the normal failure response of such tissues. Analyzing the curve profiles, however, showed a misidentification of the yield point in a few specimens, either due to a small tissue slip in the loading phase, or an abrupt load drop after tissue failure. Specifically, the yield point in specimens 90.04, 90.06, 90.08 and 90.20 was therefore specified to be equal to the ultimate strength, as criteria of a 50% drop in gradient identified a point beyond the ultimate strength. The yield point in specimens 90.05 and 90.22 was determined based on the first clear incidence of a slope reduction, as the criteria of a 50% drop passed the first clear yield point in 90.05 and identified what was clearly a slip in the sample in the loading phases in 90.22.

3.5.3 Sample conservation

After the biomechanical testing, the samples were then wrapped in saline-soaked gauze and transported in an insulated box back to the MSRU for conservation and storage in 4% Formalin until the completion of the study, at which point the samples will be archived. Due to scientific interest and more detailled analysis of the tissue reaction

triggered by TI or RI, a histological examination of the tendon samples was to follow after that study (*additional remark: histology in progress*) .

3.6 Statistical Analysis

Statistical analysis of data from macroscopic scoring, macroscopically measured distances between markers and biomechanical values was performed using a 2-tailed Student's t-test, comparing differences between the RI and TI at each timepoint as well as comparing the two timepoints for each treatment (SPSS version 23). A p-value lower than 0.05 was considered indicative of statistically detectable differences. Levene's test for equality of variance was used to establish whether equal variances were assumed or not, prior to evaluating the difference of means using Student's t-test.

4 Results

4.1 Viability / Mortality

There was no mortality observed troughout the hole study, neighter test-item related, nor otherwise.

4.2 Clinical Signs / Veterinary Examinations

All sheep tolerated the suspension system very well. Care was taken that no friction occurred between the suspension net and the surgery wound. For additional wound protection, the net was padded with cotton. Complications in wound healing noted in 90.07 (13wTI) and 90.22 (6wTI) were only superficial and not related to the treatment.

All the operated sheep showed signs of lameness during the postoperative period. The duration of lameness was varying within a range of 13 to 30 days. Most of them showed only a mild lameness, except of the sheep 90.24 (6wTI). It was moderately lame for 27 days post surgery. Furthermore, most of the animals showed signs of mild swelling. The sheep 90.14 and 90.15 (both 13wRI) exhibited moderate swelling of the surgical area, whereas a severe swelling, soft in touch, was detected in sheep 90.16 (13wTI). The swelling of 90.16 was healed after 18 days. Three sheep, 90.04, 90.06 (both 6wRI) and 90.18 (13wRI), did not show a swelling of the operated area at all *(See Appendix 8.4 Clinical abnormalities, for details about postoperative clinic)*.

Comparing the RI versus TI-treated animals, the following results can be noticed: RI-treated animals averaged 20 ± 5.5 days (mean ± standard deviation) for postoperative lameness and 10.8 ± 11.5 days for postoperative swelling. On the other hand, TI-treated sheep averaged 17 ± 5 days for lameness and 14.3 ± 4.3 days for swelling during posteroperative period.
That demonstrated a notably higher variability in duration of postoperative swelling in RI-treated animals. Next to that, no major difference between treatments was observed with regards to postoperative lameness and swelling.

All noted abnormalities responded to treatment, when treatment was needed, and were resolved in a timely manner. Aside from lameness and swelling, which are directly related to shoulder surgery, other noted abnormalities were not related to the treatment applied *(Appendix 8.4)*.

4.3 Body Weights

All animals displayed normal body weight fluctuation with time, consistent with their food intake during the experiment. There was no test item related or pathology-related change in body weight *(Appendix 8.5)*.

4.4 Surgery notes and abnormalities

Duration of surgeries ranged between 48 minutes and 1 hour 33 minutes, with an average of 1 hour 4 minutes per surgery. There was no notable effect on surgery duration based on the material used (1 hour 8 minutes on average using RI or 1 hour 0 minutes on average using TI). Anatomical or procedural abnormalities noticed during surgery by the surgeons were reported in the table below *(Appendix 8.6)*.

4.5 Technical aspects of suture material during surgery

Both suture material could be well handled during surgery. While the RI is slightly stiffer, the elasticity of the TI material made it more pleasant for the surgeon to tie the knots. Also the smaller and more rounded needle of the TI made it easier to make the stitches at the desired distance within the tendon compared to the RI with a larger and less rounded needle. Both suture materials showed good holding power during knotting. The composition of the TI rendered it easier on the hands of the surgeon when tieying the knots. The RI cut the skin of the fingers even through the latex gloves when tightening the knots. This never occurred with the TI, which made it more pleasant for handling the material.

4.6 Macroscopic evaluation and scoring

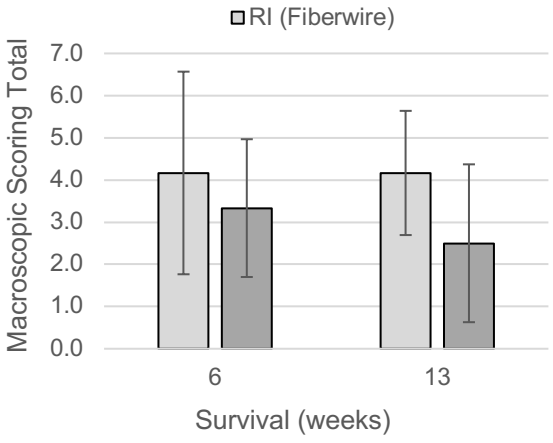


Figure 4.1: Mean macroscopic score total from n=6 specimens per group. Error bars indicate standard deviation

In the macroscopic evaluation low grades indicate more normal finding, while higher grades report more pathological findings or abnormalities. The macroscopic evaluation score sheet is shown in Appendix 8.3. The results of all macroscopic examinations and evaluations of the 24 sheep are reported in Appendix 8.8. Computing the sum of all individually scored parameters, the following results were found: The 6-week survival group scored 4.2 ± 2.4 with RI and 3.3 ± 1.6 with TI. The 13-week survival group scored 4.2 ± 1.5 with RI and 2.5 ± 1.9 with TI. These values are depicted in Figure 4.1. Differences between groups were statistically not significant.

When analyzing the individual parameter scores, two statistically detectable differences were found: First of all, the 13-week survival group treated with TI was the only group without inflammation at the stitch. In all the other 3 groups inflammation at the stich was present *(Table 4.1)*. From a statistical standpoint, the difference between inflammation at the stitch in the TI-treated 6-week group (0.67 ± 0.516) and the TI-treated 13-week group (0.00 ± 0.00) was significant (p=0.025).

A second statistically detectable difference was also notable when analyzing the fibrosis parameter. Indeed, the severity of fibrosis was higher in the RI-treated groups, regardless of survival time *(Figure 4.2)*. The difference in fibrosis between the RI-treated and TI-treated 13-week survival groups was statistically significant (p=0.002).
During stepwise dissection and macroscopic evaluation additional notes were made about details of observational findings and other not anticipated lesions. It is noticeable that findings like “fibrous tissue attachments to the tendon are milder” (90.08 13wTI), “less of a fibrous bump” (90.12 13wTI), “well healed”, “new tissue looked like tendon” (90.16 13wTI) or “not much adhesion” (90.20 6wTI) were found in TI-treated animals. On the other hand, many notes about fibrosis and attachment were detected in RI-treated animals: “more fibrosis in general” (90.02 6wRI), ”more adhesions” (90.03 6wRI), “more fibrosis (…) more adhesions” (90.05 6wRI), “more fibrosis” (90.14 13wRI), “very fibrotic” (90.15 13wRI) or “more adhesive than usual” (90.17 13wRI). Furthermore two RI-treated animals showed signs for necrotic tendon tissue (90.03 6wRI, 90.05 6wRI). Comments about plate loosening were recorded in four specimen, all of them were treated with RI. No findings about plate loosening in TI-treated sheep were found (s*ee Appendix 8.8 for all additional findings*).

Group	Hematoma (0 - 1)	Inflammation (0 - 3)	Tendon Visibility (0 - 1)	Fibrosis (0 - 2)	Tendon Thickness (0 - 2)	Tendon tearing (0 - 1)
RI, 6 weeks	0.17 ± 0.41	0.33 ± 0.82	0.00 ± 0.00	0.83 ± 0.41	0.83 ± 0.41	0.17 ± 0.41
TI, 6 weeks	0.17 ± 0.41	0.00 ± 0.00	0.00 ± 0.00	0.67 ± 0.52	1.33 ± 0.52	0.00 ± 0.00
RI, 13 weeks	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	1.17 ± 0.41	1.50 ± 0.84	0.00 ± 0.00
TI, 13 weeks	0.00 ± 0.00	0.00 ± 0.00	0.17 ± 0.41	0.17 ± 0.41	1.67 ± 0.52	0.00 ± 0.00

Group	Gap (0 - 1)	Suture tearing (0 - 1)	Suture cheesewiring (0 - 1)	Inflammation at stitch (0 - 3)	Knot security at plate (0 - 2)	Prox bone tunnel widening (0 - 1)
RI, 6 weeks	0.33 ± 0.52	0.00 ± 0.00	0.33 ± 0.52	1.00 ± 0.89	0.00 ± 0.00	0.17 ± 0.41
TI, 6 weeks	0.00 ± 0.00	0.00 ± 0.00	0.17 ± 0.41	0.67 ± 0.52	0.00 ± 0.00	0.33 ± 0.52
RI, 13 weeks	0.00 ± 0.00	0.00 ± 0.00	0.50 ± 0.55	0.67 ± 0.82	0.00 ± 0.00	0.33 ± 0.52
TI, 13 weeks	0.00 ± 0.00	0.00 ± 0.00	0.33 ± 0.52	0.00 ± 0.00	0.00 ± 0.00	0.17 ± 0.41

Table 4.1: Macroscopic scoring individual parameter values, separated by treatment group. Low grades indicate a more normal phenotype while higher grades indicate pathological findings or abnormalities. Values are depicted as the mean ± standard deviation from n=6 specimens per group.

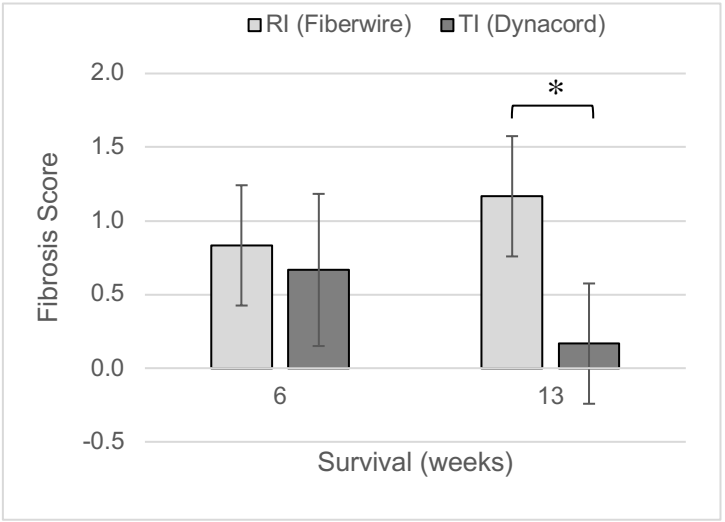


Figure 4.2: Fibrosis score mean from n=6 specimens per group. Error bars indicate standard deviations. (*) indicate a statistically detectable difference (p=0.002).

4.7 In vivo and ex vivo measurements

During specimen preparation at sacrifice the measurements detecting different distances between markers were performed. All markers (steel wire loops and screws) were found. Location of the steel wire loops was likely more difficult to find in RI-treated animals due to more fibrotic tissue (90.02 6wRI, 90.03 6wRI, 90.15 13wRI and 90.17 13wRI). In specimen of 90.15 (13wRI) caudal distal steel wire loop was not visible, but palpable. Furthermore, the cranial proximal loop was loose. That marking point could not be used for measuring, so following distances are missing for that one specimen: between the two cranial loops, between the two proximal loops and between cranial screw and cranial distal steel wire loop.

The gap size was measured directly after tendon transection during surgery. An average of 5.6 ± 1.3 mm for all 24 animals was detected. The gap size measured after suturing and prior to tightening the repair was on average 8.9 ± 1.7 mm for all 24 sheep, which detects an increase of gap size for each animal. Interestingly, in the RI-treated group (6-week and 13-week pooled), the average gap size after handling (after tendon suturing and suture shuttling, prior to tightening) was 9.8 ± 1.7 mm. This value was statistically lower in the TI-treated group (6-week and 13-week pooled), averaging 8.0 ± 1.2 mm. That difference was statistically significant ($p=0.008$), potentially indicating tendon handling and/or perceived suture elasticity while performing a repair using RI further widens the gap in a transected tendon compared to TI-repair.
All remaining measurement values were analyzed by calculating the change in value from the measurement taken on sacrifice day and the measurement taken on surgery day.

$$\text{Delta Value (mm)} = \text{Sacrifice Day Value (mm)} - \text{Surgery Day Value (mm)}$$

All values which were taken on the surgery and sacrifice day including the calculated delta values are reported in Appendix 8.9 for all 24 animals.

The distance between the marking screws was measured during surgery as well as on the sacrifice day. Analysis of the delta values of these measurements gives an evaluation of the repeatability of the measurement technique by the operator. All surgeries and measurements were performed only by one person (Prof. Brigitte von

Rechenberg). The mean Delta Value between the two marking screws was 0.4 ± 1.6 mm. As the marking screws were not expected to change in position with time, the Delta Value for the distance between marking screws was expected to be 0 mm. Any deviation from 0 mm could therefore was taken as an overall indication of the measurement accuracy variation, due to caliper and tissue handling by this operator. The Delta Value was also influenced by the size of the slot where the screw driver was inserted which was not a pin point, but a hexagonal 0.972 mm slot. The measurement accuracy was also affected by the fibrosis covering the surgical site (ex vivo).

The distance from the caudal screw to the distal marking steel wire loop increased in the RI-treated 13-week group by 9.1 ± 3.8 mm. The increase in the same distance was smaller in the TI-treated 13-week group with only 4.4 ± 2.6 mm. This difference was statistically significant ($p=0.032$).

The distal tendon width increase in the RI-treated 6-week group (11.1 ± 2.1 mm) was significantly higher than the increase in the TI-treated 6-week group (6.3 ± 2.4 mm, $p=0.004$) and also higher than the increase in the RI-treated 13-week group (7.1 ± 3.0 mm, $p=0.022$).

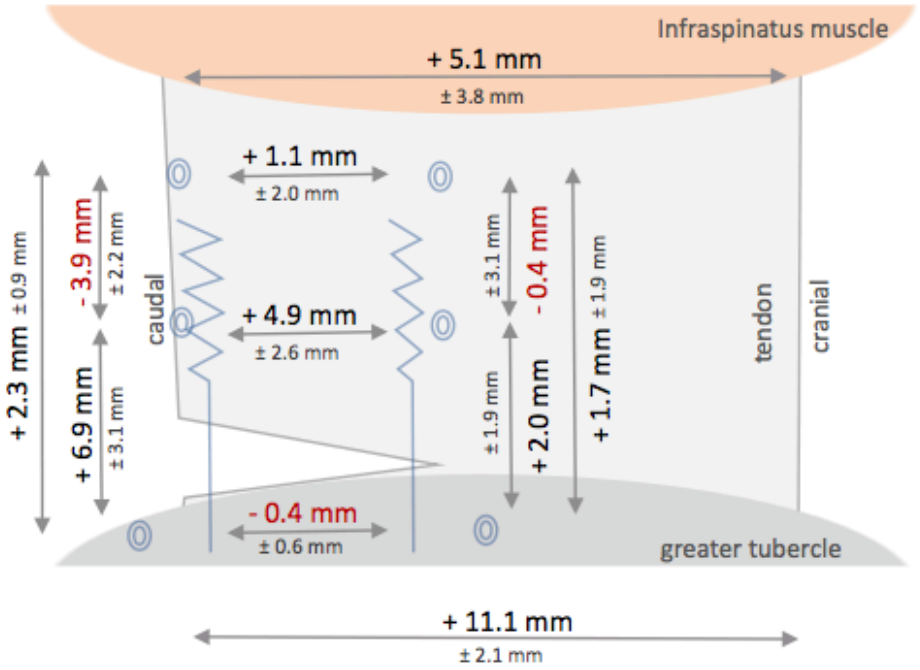


Figure 4.3.1: Delta values from 6-week group treated with RI. Means ± standard deviations reported from n=6 specimens

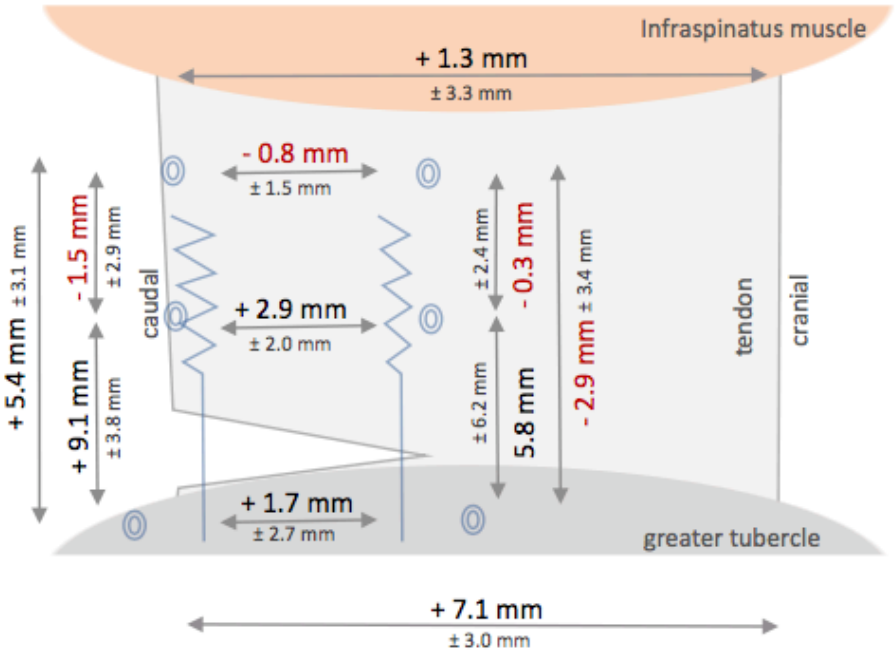


Figure 4.3.2: Delta values from 13-week group treated with RI, reported as means ± standard deviations. Delta values involving the cranial proximal steel loop marker are reported from n=5 specimens. All other delta values are from n=6 specimens

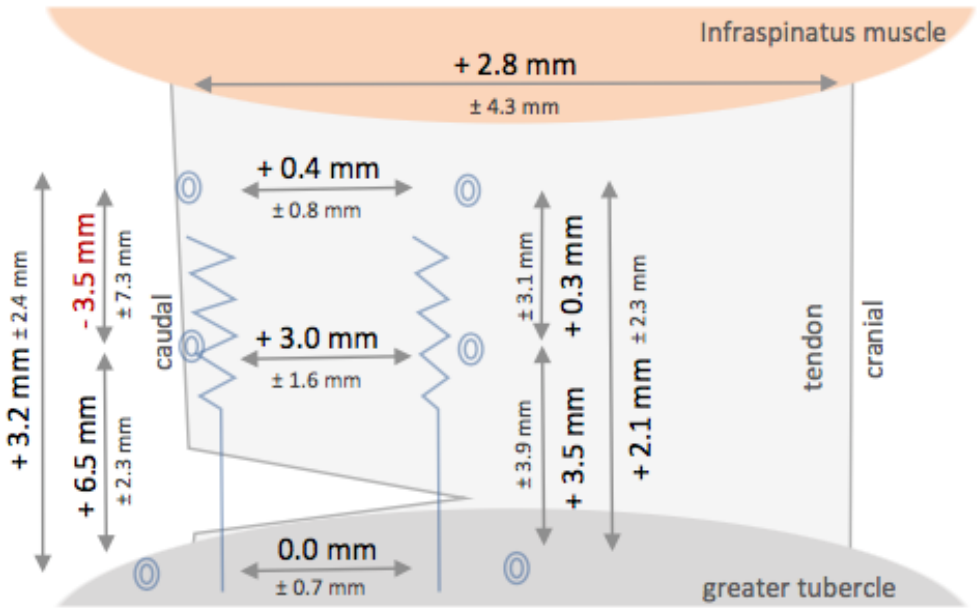


Figure 4.3.3: Delta values from 6-week group treated with TI.
Means ± standard deviations reported from n=6 specimens

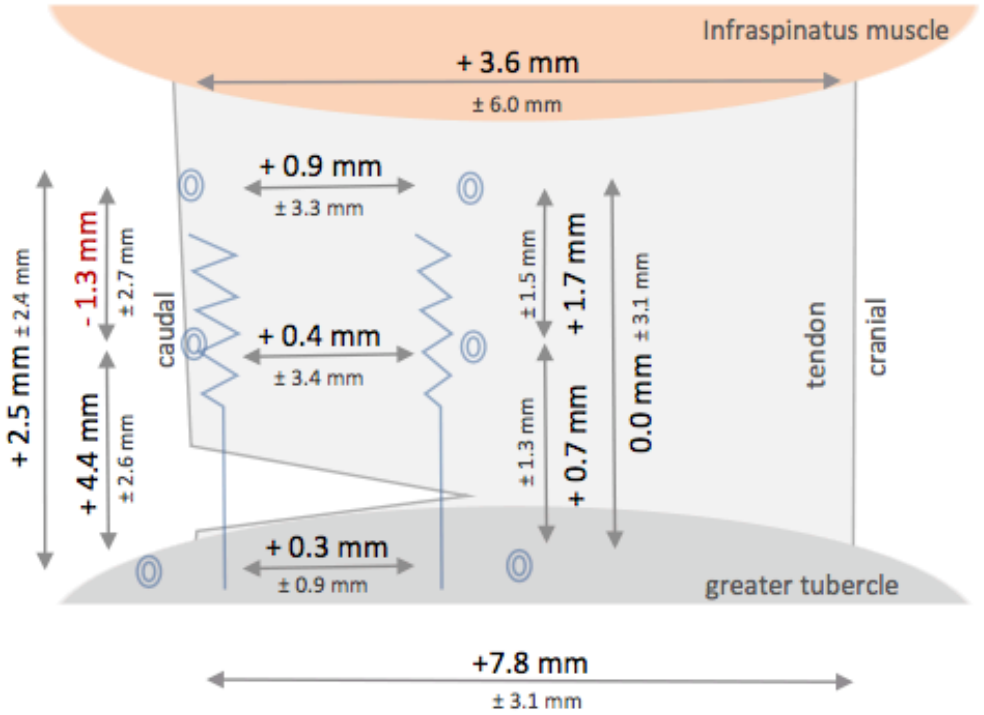


Figure 4.3.4: Delta values from 13-week group treated with TI.
Means ± standard deviations reported from n=6 specimens

Figures 4.3.1, 4.3.2, 4.3.3 and 4.3.4 depict Delta Value increase in black text with „+“ and decreases in red text with „-“. Values are reported on the same schematic shown in Appendix 8.2 and indicate means ± standard deviations.

4.8 Biomechanical testing

All samples were tested for biomechanical properties. Different test led to the evaluation of following parameters: Apparent stiffness (using non-destructive and destructive loading curves), ultimate strength and yield point. Mean values of all the 24 samples are reported in the table below. The individual values for all animals are reported in Appendix 8.10.

Group	Non-Destructive Apparent Stiffness (N/mm)	Destructive Apparent Stiffness (N/mm)	Ultimate Strength (N)	Yield Point (N)
6-week, RI	56 ± 17	91 ± 35	643 ± 450	592 ± 449
6-week, TI	41 ± 6	74 ± 19	622 ± 183	594 ± 196
13-week, RI	46 ± 14	113 ± 18	1072 ± 412	942 ± 941
13-week, TI	48 ± 11	111 ± 30	1111 ± 350	1039 ± 280

Table 4.2: Stiffness, strength and yield point means ± standard deviations from n=6 specimens per group.

Figures 4.7.1, 4.7.2, 4.7.3 and 4.7.4 respectively depict means with error bars showing standard deviations for apparent stiffness derived from non-destructive cyclic loading curves, apparent stiffness derived from the load to failure curve, ultimate strength and yield strength.

Statistically significant differences were found by comparing the two TI-treated groups. Destructive apparent stiffness ($p=0.031$), ultimate strength ($p=0.013$) as well as yield point ($p=0.01$) were all higher in the 13-week group compared to the 6-week-group in TI-treated animals.

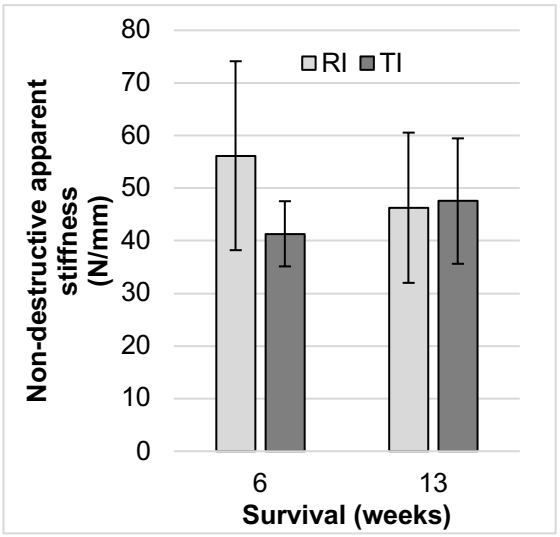
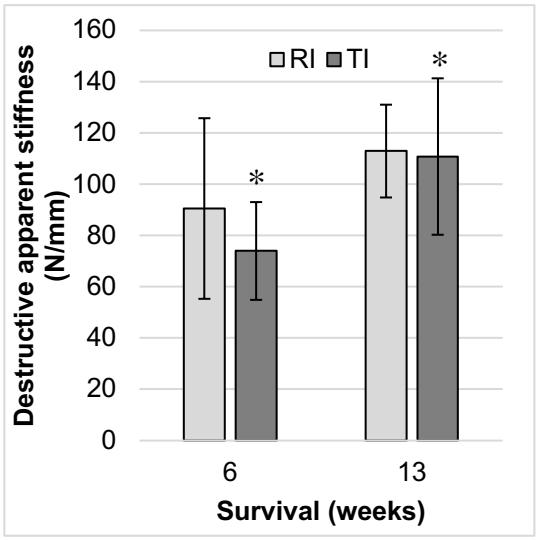
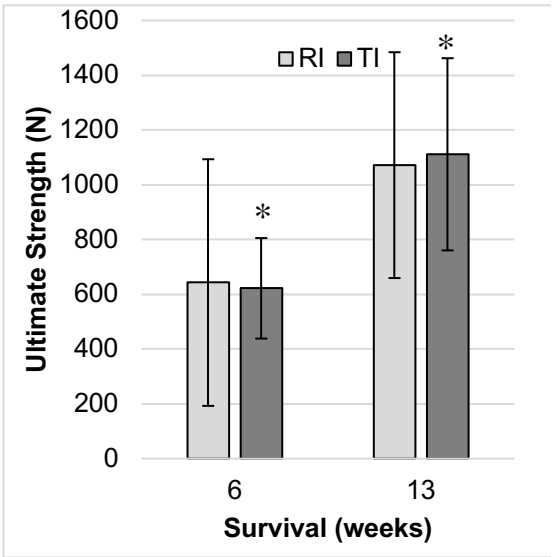


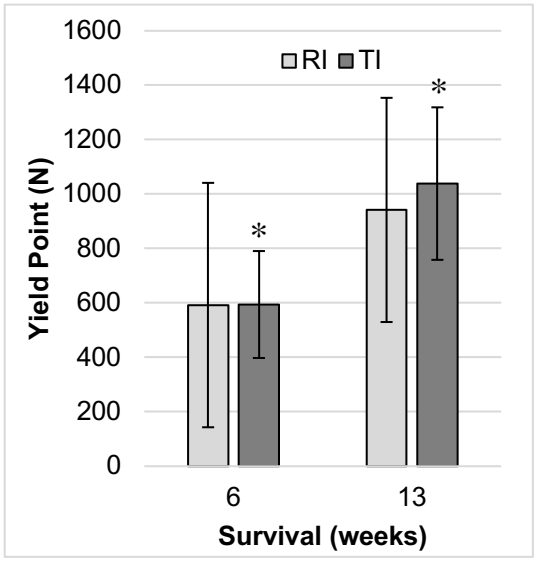
Figure 4.4.1: Mean non-destructive apparent stiffness from n=6 specimens per group. Error bars indicate standard deviations.



4.4.2: Mean destructive apparent stiffness from n=6 specimens per group. Error bars indicate standard deviations. A statistically detectable difference (p=0.031) was found between groups marked with (*).



4.4.3: Mean ultimate strength from n=6 specimens per group. Error bars indicate standard deviations. A statistically detectable difference (p=0.013) was found between groups marked with (*).



4.4.4: Mean yield point from n=6 specimens per group. Error bars indicate standard deviations. A statistically detectable difference (p=0.01) was found between groups marked with (*).

Figure 4.5: Incomplete transection of native tendon tissue in specimen 90.09 (left) and 90.13 (right). Remaining bundles of native tendon still apparent after mechanical testing are shown with black arrows.

Notably, during the mechanical testing procedure of specimen 90.09 (13wTI), the bone failed before the tendon tissue. After further dissection, an approximately 3 mm bundle of intact tendon fibers was found at the transection region *(Figure 4.5 left)*. That is an indication the intact part of the tendon tissue was not completely transected during preparation. An incomplete intact tissue transection was also detected in specimen 90.13 (13wRI) *(Figure 4.5 right)*, although the bone did not fail before the tendon tissue during the biomechanical testing of this specimen. This incorrect preparation would likely increase the apparent stiffness and ultimate strength. However, for the purposes of this thesis all data are included in the statistical analyses.

5 Discussion and conclusion

Overall, no anesthesia complications or mortality due to surgery was observed in any animal. Furthermore, the postoperative suspension system was tolerated without any problems. Bodyweight fluctuation were within normal range. Both groups, TI- and RI-treated animals, showed no difference in postoperative lameness and swelling, so no negative effect related to TI treatment was observed. Most of the animals showed only a mild lameness and swelling, which can be assessed as normal clinical observations after any surgical treatment. Only two 13wRI-treated sheep (90.14 and 90.15) showed a moderate swelling of the operated area. Interestingly, in these two sheep more fibrosis than usual was observed during macroscopic evaluation. On the other hand, in one 13wTI-treated animal (90.16) a severe swelling, soft in touch, was found. However, in that specimen the tendon showed good healing, especially at the tendon undersite. The new tissue looked like tendon tissue. Comparing the duration of swelling, animals of RI-group exhibited a higher duration than animals of TI-group.

Studying the procedure at surgery and sacrifice day itself, several conclusions can be made. For most of the animals, surgery went very well and without any complications.
Based on the knowledge captured during pilot studies, the surgical technique could be done with accuracy and a high standardization. A single-row repair with modified Mason-Allen stitch is known as a strong suture technique without causing necrosis, with a good biological toleration[52,67]. As there is a correlation between vascularization and healing, the stitches should respect the bloodflow of the tendon tissue[7]. To improve the outcome, a cortical-bone-augmentation can be added to protect the repair and minimized the rate of failure[2,52,70]. During surgeries of that study a 7-hole-plate was used with success. Due to lower risk of retear, the study was done by reparing a partial thickness tear instead of a fullthickness tear[9,10,92]. Although nowadays the arthroscopic approach is the standard of care for rotator cuff repair, the open approach was used for different reasons. First of all, suture techniques like the modified Mason-Allen stitch is rarely used via arthroscopy. Multiple transtendinous passes are more difficult to make by arthroscopy approach[67]. Furthermore measuring by caliper and propper documentation by photography would not be possible without an open approach, as well as getting the right angle for drilling the bone tunnels is a lot easier through an open approach.

Fibrewire was selected as reference item, because it is a commonly used suture material in rotator cuff repair. Compared to other suture material, which are used for shoulder surgery, Fibrewire showed superior results. A critical point is the high stiffness of that suture material. It guarantees a stable repair, but also can lead to the so called cheesewiring-effect, which means suture material cutting through the tendon tissue. That may cause failure of repair[71].

Abnormalities noted during surgery did not translate into problematic findings at sacrifice. For example, in specimen 90.06 (6wRI) the plate was a bit loose during surgery, even after suturing. That could not be confirmed at sacrifice day, the plate was firm. During surgery of 90.15 (13wRI) the drill bit broke and was left in the bone. No negative effects could be observed during ex-vivo evaluations. Finally, in sheep 90.20 (6wTI) surface of the cranial part of the tendon was covered by a part of the supraspinatus muscle at the time of sacrifice. To achieve correct measurements, the tissue needed to be freed from adhesions. That tissue manipulation did not, as originally thought, correlate with a higher fibrosis, but a cyst-like tissue was observed between the tendon and the fascia. Overall, the abnormalities noted during surgeries did not seem to impact the healing or performance of the RI or TI, based on the macroscopic evaluation at sacrifice.

During surgery, the surgeon noticed good handling for both suture materials, TI and RI. As the TI is more elastic and not as stiff as the RI, knot tying and handling is more pleasant with TI. RI cuts the skin of the fingers of the surgeon even through the gloves. This did not happen with TI. Next to that, the needle of TI is smaller and more rounded than the RI needle, which makes it easier to stitch accurately. There is no difference in knot holding security between the suture materials. Several investigators pointed out the main important characteristics of a good suture material. Good handling, knot and loop holding security and elasticity were some of these points corresponding with our surgeon's opinion[68,74,76-78]. A risk of using suture material with a high stiffness is tissue damaging and repair failure by cutting through the tissue[75].

Also the evaluation procedure during sacrifice went very well. For an optimal repeatability, every evaluation was done by one person (Prof. Dr. Brigitte von Rechenberg). All markers (steelwire loops and screws) were found. RI-treated animals

showed notably more fibrosis during macroscopic evaluation, which led to more difficulties in locating the markers. The distance between the marking screws was not expected to differ between measuring at surgery and sacrifice day. Therefore, evaluation of these parameters gives information about the measurement accuracy variation. That value is affected by caliper and tissue handling, as well as fibrosis covering the tissue and the slot of the screw where normally the screw driver is inserted. The mean Delta Value between the two marking screws was 0.4 ± 1.6 mm, which verifies an accurate and repeatable evaluation system for distance measurement.

Regarding macroscopic scoring, TI-treated animals showed a tendency to score lower overall (the lower, the more normal) at 13 weeks compared to RI-treated animals, albeit not to a statistically significant extent. The inflammation at the stitch was overall lower in TI-treated animals, which also exhibited less variability for this parameter. Furthermore, fibrosis was notably higher in RI-treated animals at 13 weeks, compared to TI-treated animals. Next to the scoring sheet, additional findings of macroscopic evaluation were noted. For specimen of RI several informations about fibrosis and adhesions were made. During surgery some animals exhibited more bleeding than usual. This could indicate a tendency for more fibrosis; however, this was not systematically observed. Indeed, for example, excessive bleeding was observed during the surgery of 90.03 and 90.04 (both 6wRI). At sacrifice 6 weeks later, in 90.03 a larger area of fibrosis was noted, albeit still moderate. In 90.04 sacrificed also 6 weeks after surgery, fibrosis was mild. The link between excessive bleeding and fibrosis was therefore not established. Next to that, plate loosening and necrotic tissue was mentioned for RI-treated animals. TI-group specimen did not show any plate loosening.

A parameter for evaluating the tissue reaction triggered by suture material is the gap size. As it is difficult to avoid, gap size increased during surgery due to tissue manipulating and suturing. All specimen showed gap widening, though gap size increase was higher in RI compared to TI specimen. A conclusion is that TI is characterized by better handle-ability, less tissue manipulations, better elasticity and facilitating knot tightening. The tissue reaction was further evaluated by looking at measurements taken during surgery and after sacrifice. The increase in distance between the caudal screw and the caudal distal steel wire loop marker is an indication for tendon retraction at the repair site. This was indeed found to be higher in the RI-treated group

at 13 weeks, compared to the TI-treated group. Interestingly, the same group also showed an increased fibrosis. It is difficult to define the cause and the effect. It may be that the fibrosis came after the retraction as a scar-forming response. On the other hand, it is possible that the fibrotic tissue, which is weaker than healthy tissue, caused more retraction. The correlation with a higher incidence of cheesewiring could not be established. Regarding to that, it needs to be pointed out, that the definitive detection of cheesewiring during macroscopic evaluation at sacrifice was difficult to achieve without destroying the tendon tissue itself. Therefore, it may be a notable incidence of false negatives.
Furthermore, measurement analysis showed that the RI-treated 6-week group exhibited notable tendon width increase. This increase is interesting to note in relation to the biomechanical findings of the RI-treated 6-week group. While there was no perceived difference in stiffness between the RI and TI-treated groups at 6 weeks, taking the increased tendon width into account may point to an overestimation of stiffness for the RI-treated 6-week group. This is difficult to quantify, as the issue of load normalization is a known limitation when testing soft tissues with varying cross-sections.

Last step of evaluation was the testing of biomechanical properties of the healed tendon tissue. The healthy half of the tendon was transsected prior to testing, to make sure that only healed tendon tissue was analized. That step is really important. The extent of transection followed clear guidelines but could not be accurately standardized. Cutting less or too much of the tendon could influence the results of biomechanical testing. In case of remaining healthy tendon bundles an overestimation of biomechanical properties of repaired tissue would occur. The opposite, cutting repaired tendon tissue by mistake, would lead to an undererstimation of biomechanics. The variability, by design, did not favor a group over another, as all tendons were processed similarly for biomechanical testing. Testing the healed portion of the tendon alone, by transecting the native portion, was however necessary. Indeed, if the entire tendon were left intact prior to mechanical testing, the native portion would mainly reflect the mechanical properties of the tissue as a whole, making potential differences in the biomechanics of the healed tissue impossible to detect.

Evaluating the data of biomechanical testing, interesting conclusions can be made. First of all, within the TI-treated group functional improvements from week 6 to week 13

were observed. Stiffness, yield point and ultimate strength improved notably. This is a clear sign for tissue healing response leading to an increase of strength and stiffness within healing period. In that time the third phase of tendon healing takes place: remodeling/ maturation. During that period the reorganization of collagen occurs[35,38]. Our biomechanical findings match with postoperative rehabilitation recommendations of human orthopedics. For strenghthening exercises, normally starting at week 10-12 post surgery, these growing tissue functions are necessary. The clinical outcome of tendon healing depends on mechanical environment. During early healing heavy load bearing should be avoided and level of activity should be chosen carefully. Optimal is controlled loading. Neighter total immobilization, nor overuse is recommended[50,51]. It is important to note that human patients are likely more responsive and compliant to postoperative medical recommendations than sheep. To avoid total weightbearing on the shoulder during early healing period, the sheep hang in a suspension system. Active range of motion was possible, with guaranteed prevention of overuse.

Another important finding of biomechanical evaluation was the increased variability in biomechanical values for 6-week RI-treated group, compared to TI specimens. The lower the variability, the more accurately the prognosis of repair outcome. This lower variability in outcomes was seen across evaluation methods for the TI-treated group.

Overall, specimen of RI-treated group showed more fibrosis, more instances of cheesewiring, even though not statistically detectable, as well as macroscopic signs of necrosis under some sutures and more remodeling of repaired tissue. On the other side, in TI-treated animals a more organized new tendon-tissue structure and morphology was observed. Furthermore, there was less macroscopic evidence of necrosis and less remodeling. Comparing TI-treated animals, stiffness, yield point and strength showed lower values at early timepoint (6 weeks) compared to evaluation 13 weeks post surgery.

Concerning the results of TI-treated animals, a correlation between healing of tendon structure and clinical outcome can be made. Though healed tendon tissue will never achieve biomechanical properties of healthy tissue, the functional outcome may improve towards normal[35,38]. It is known that torn tendons with changed tissue structure and composition have suboptimal healing potential[5,48]. Torn tendon fibres are not able to

participate in load sharing. On the one hand that lead to decreased tensile mechanical properties of the whole tendon, on the other hand it could increase the risk for repair failure. The remaining intact tendon tissue needs to compensate the missing power of torn fibres to stabilize loads of the shoulder. That could cause overloading resulting in tendon retear[24,25]. An other investigator also confirmed the correlation between tendon healing, postoperative strength and evaluation of clinical outcome ranged with the constant score, a clinical parameter for describing post-operative outcome[34]. Other important factors influencing biomechanical results and clinical outcome are inflammation and fibrosis. Controlled inflammation is a necessary step within the tendon healing procedure. Due to inpropriate termination of inflammatory reaction, a persistent inflammation can occur. Main consequence is the excessive production of fibrous tissue, which will lead to adhesion formating. Degenerative scar-tissue with decreased mechanical properties and risk of retear, as well as inhibition of natural gliding of tendon in the tendon sheath can result[40-42].

Next to the already mentioned risk factors, the cheesewiring-effect is a main problem causing failure of repaired tendon tears. As already explained, the higher the stiffness of a suture material, the higher the risk of cheesewiring. Fibrewire is known for that disadvantage. In addition, necrosis under the stitches was also more observed with Fibrewire. The cheesewiring-effect and necrosis most likely explains the fact that retear in clinical cases is often seen around 6 weeks after surgery. Beeing more elastic, Dynacord shows somehow a tissue-protective character, such that necrosis and cheesewiring may be prevented while still due to the silicone core the tendon gap closes over time.

Based on that, it can be concluded that surgeries done with Dynacord suture material could lead to better clinical outcome due to better tendon tissue healing and less fibrosis. Furthermore there is lower risk for repair failure by tendon retear according to cheesewiring or failed torn tendon fibres.

As a limitation it should be mentioned that detaching followed by the immediate reattaching of the ovine tendon does not represent the clinical picture[108]. Most of the operated human patients suffered from nonacute tears[33]. As there are important similarities between the ovine and the human rotator cuff, the sheep model is a good and necessary step in shoulder research[11]. It is a relatively rapid way to investigate rotator cuff repair options, identify mechanism of healing and answer clinically relevant

questions in an acute model[11,108]. Factors keeping in mind regarding animal models are biologic, metabolic, hormonal and anatomical differences from humans, as well as noncomplience during healing period[35]. Characteristics of a model is the homogeneity. The age, body size and weight of the 24 sheep were relatively equal, as well as all sheep were female, had the same limb operated in the same standardized way. That allows perfect comparison of the macroscopic scoring and biomechanical values afterwards, succeeding in comparison of the two suture materials. Because of beeing quadrupeds, the sheep's shoulder joint is weightbearing in contrast to the humans. That results in a way higher load on the operated limb during healing period than in human patients[101]. Due to that fact, current rotator cuff sheep model can be used to reconstruct patients overuse of operated shoulder postoperatively.

Evaluating all the clinical and biomechanical results, the test item Dynacord™ showed at least equal results compared to the reference item Fibrewire®. Regarding overall tissue regeneration we could detect better results for the newly developed suture material Dynacord™ with less risk of necrosis, fibrosis or inflammation.

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7 Glossary

6wRI	6 week reference item group
6wTI	6 week test item group
13wRI	13 week reference item group
13wTI	13 week test item group
BID	Two times a day
BW	Bodyweight
cm	Centimeter
ETHZ	Eidgenössische Technische Hochschule Zürich
i.m.	Intramuscularly
IU	International unit
i.v.	Intravenously
kg	Kilogram
mg	Milligram
ml	Milliliter
mm	Millimeter
mm/s	Millimeter per second
MSRU	Musculoskeletal Research Unit
N	Newton
N/mm	Newton per millimeter
N/s	Newton per second
OP	Operation
PMMA	Polymethylmethacrylat
RI	Reference item
s.c.	Subcutaneously
SID	Once a day
TI	Test item

8 Appendix

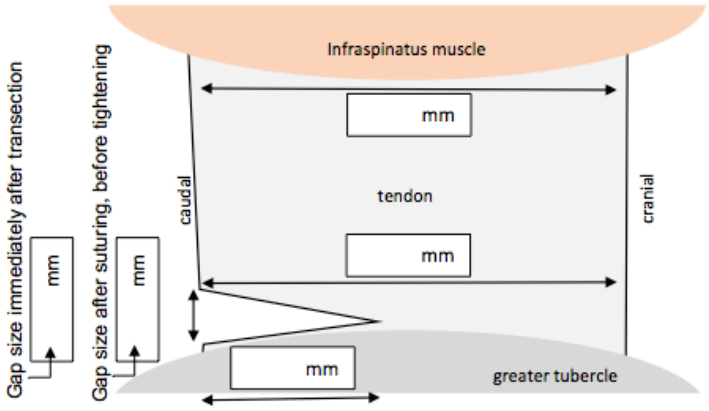
8.1 Treatment allocation

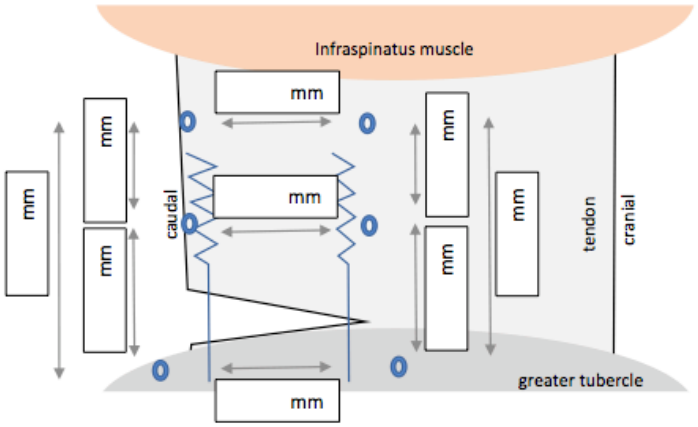
Animal number	Treatment	In-Life Duration Post OP (weeks)
90.01	RI	6
90.02	RI	6
90.03	RI	6
90.04	RI	6
90.05	RI	6
90.06	RI	6
90.07	TI	13
90.08	TI	13
90.09	TI	13
90.10	RI	13
90.11	TI	13
90.12	TI	13
90.13	RI	13
90.14	RI	13
90.15	RI	13
90.16	TI	13
90.17	RI	13
90.18	RI	13
90.19	TI	6
90.20	TI	6
90.21	TI	6
90.22	TI	6
90.23	TI	6
90.24	TI	6

8.2 Measurement sheet

MSRU0090 Measurement sheet
Animal: Evaluated by (Initals):
Filled by (Date/Initials):

University of Zurich





8.3 Macroscopic Evaluation Score Sheet

MSRU0090 Macroscopic Evaluation Scoring Sheet
Animal: Evaluated by (Initals):
Filled by (Date/Initials):

University of Zurich[UZH]

Task	☑ Grade	Comments (note unanticipated lesions incl. location and severity)
First impression	**Hematoma** ☐ 0 no ☐ 1 yes **Inflammation** ☐ 0 none ☐ 1 mild ☐ 2 moderate ☐ 3 severe **Tendon** ☐ 0 visible ☐ 1 non-visible **Fibrosis** ☐ 0 mild ☐ 1 moderate ☐ 2 severe	
When tendon exposed	**Tendon thickness** ☐ 0 thin ☐ 1 normal ☐ 2 thicker **Tendon** ☐ 0 intact ☐ 1 retorn **Gap** ☐ 0 no ☐ 1 yes **Suture** ☐ 0 intact ☐ 1 torn **Suture cheese wiring** ☐ 0 no ☐ 1 yes **Inflammation at stitch** ☐ 0 none ☐ 1 mild ☐ 2 moderate ☐ 3 severe **Knot security at plate** ☐ 0 firm ☐ 1 partially open ☐ 2 open **Bone tunnel proximal** ☐ 0 normal ☐ 1 widenend	

8.4 Clinical Abnormalities

Animal number	Post-OP lameness (days)	Post-OP swelling (days)	Other Clinical Abnormalities
90.01	15	11	-
90.02	17	13	Post-OP swollen area soft to the touch, likely fluid-filled.
90.03	16	5	-
90.04	16	0	-
90.05	19	18	-
90.06	16	0	Small pea-size abscess near right shoulder noticed during acclimatization, not in the surgery area, treated with curettage and Betadine solution, controlled regularly, healed on 20.6.17
90.07	13	10	Complications in wound healing post OP noticed 18.07.17, exudation around distal stitches, the end of the suture material which was sticking out (likely cause) was shortened and the wound was treated with Betadine solution and controlled regularly. The wound was healed on 25.09.17.
90.08	13	7	-
90.09	13	11	-
90.10	15	39	Infection with Parapoxvirus ovis (“Lippengrind”) noticed on 21.06.17 during acclimatization period, treated with Betadine solution and controlled regularly, progress of healing was good, healed on 30.06.17. During surgery prep one hoof was cut too deep (left hindlimb), bandage placed for 2 days. Reduced appetite in the first days after OP, diarrhea 2 days post OP (lasting only one day).
90.11	15	24	Infection with Parapoxvirus ovis (“Lippengrind”) noticed on 20.06.17 during acclimatization period, treated with Betadine solution, controlled regularly, progress of healing was good, healed on 30.06.2017. Reduced appetite in the first days after surgery.
90.12	17	16	Diarrhea 29.6.17 and 30.6.17. Abscess right shoulder, healed on 20.06.17. Rectum prolaps from 9.7.17 to 9.8.17: Rectum prolapse noticed on 9.7.17. Under local anesthesia, rectum was repositioned and a purse-string suture around the anus was made. A “Bühner”-needle was used for that treatment. Sheep was treated with analgetic/ anti-inflammatory medication and was regularly observed. After treatment, the defecation went well and the general condition of the sheep was good. For this treatment, sheep was given Medetomidin (0.56 mg i.m. on 09/07/17, 0.85 mg i.v. on 10/07/17), Buprenorphine (1.13 mg i.m. on 09/07/17), Atipamezol (2.8 mg i.m. on 09/07/17, 4 mg i.v. on 10/07/17), Carprofen (225 mg s.c. on 09/07/17 and 10/07/17 and 11/07/17), Lidocain/Morphine (60 mg / 5.6 mg Epidural, 10/07/17).
90.13	20	4	-
90.14	20	4	-
90.15	30	13	Abscess caudal of right scapula, pea size, not open, no treatment necessary

Animal number	Post-OP lameness (days)	Post-OP swelling (days)	Other Clinical Abnormalities
90.16	15	18	Post-OP swollen area soft to the touch, likely fluid-filled.
90.17	28	22	-
90.18	28	0	-
90.19	15	13	-
90.20	15	13	-
90.21	15	13	-
90.22	19	17	Little exudation ventral part of stitches starting on 13.09.17, no treatment necessary, healed on 16.09.17
90.23	27	15	Reduced eating in the first week post OP
90.24	27	15	-

8.5 Body Weights

Animal number	Bodyweight 1	Bodyweight 2	Bodyweight 3	Bodyweight 4
90.01	50.0 kg/ 24.05.17	-	-	-
90.02	50.0 kg/ 24.05.17	-	-	-
90.03	47.8 kg/ 24.05.17	-	-	-
90.04	50.2 kg/ 24.05.17	-	-	-
90.05	49.4 kg/ 24.05.17	-	-	-
90.06	50.6 kg/ 24.05.17	-	-	-
90.07	52.2 kg/ 14.06.17	57.2 kg/ 25.09.17	-	-
90.08	53.05 kg/ 20.06.17	56.2 kg/ 25.09.17	-	-
90.09	49.6 kg/ 20.06.17	57.9 kg/ 25.09.17	-	-
90.10	54.6 kg/ 14.06.17	61.5 kg/ 25.09.17	-	-
90.11	56.8 kg/ 20.06.17	64.4 kg/ 25.09.17	-	-
90.12	48.8 kg/ 24.05.17	63.5 kg/ 21.06.17*	56.5 kg/ 09.07.17	61.8 kg/ 25.09.17
90.13	46.5 kg/ 29.06.17	50.2 kg/ 06.07.17	54.0 kg/ 06.10.17	-
90.14	49.7 kg/ 29.06.17	55.5 kg/ 06.07.17	58.3 kg/ 06.10.17	-
90.15	50.8 kg/ 29.06.17	53.3 kg/ 06.07.17	59.6 kg/ 06.10.17	-
90.16	49.2 kg/ 29.06.17	50.3 kg/ 06.07.17	59.2 kg/ 06.10.17	-
90.17	55.9 kg/ 29.06.17	57.6 kg/ 09.07.17	61.5 kg/ 06.10.17	-
90.18	51.8 kg/ 29.06.17	52.8 kg/ 09.07.17	57.3 kg/ 06.10.17	-
90.19	57.1 kg/ 21.08.17	60.4 kg/ 06.10.17	-	-
90.20	59.9 kg/ 21.08.17	60.5 kg/ 06.10.17	-	-
90.21	59.9 kg/ 21.08.17	57.3 kg/ 06.10.17	-	-
90.22	59.9 kg/ 21.08.17	67.5 kg/ 12.10.17	-	-
90.23	61.9 kg/ 21.08.17	64.0 kg/ 12.10.17	-	-
90.24	63.0 kg/ 21.08.17	63.0 kg/ 12.10.17	-	-

* wrong entry at day of measuring

8.6 Surgery Anormalities

Animal number	Surgery Duration (h:mm)	Surgery Procedure Notes/Abnormalities
90.01	1:33	One of the cranial steel suture loops placed close to the corner of the transection instead of midway within the suture row
90.02	1:00	Bone tunnel exits close to each other so shuttle suture was wrapped around drill bit when making new tunnel. Shuttle suture was replaced. No additional tunnels were drilled.
90.03	1:20	Bleeding more than 90.01 or 90.02, could cause more fibrosis
90.04	1:02	Bleeding more than usual; about 3 mm longitudinal split of the tendon tissue between suture rows
90.05	0:58	-
90.06	1:01	Plate is a bit loose (about 1 mm), tightening it further would have closed the gap so it was not possible to tighten more
90.07	1:11	-
90.08	1:14	Tendon is thinner than usual (not in width)
90.09	0:53	-
90.10	0:52	Additional steel suture marker was added to the corner of the transection (drawn in schematic) in order to indicate end of transection at sacrifice
90.11	0:57	-
90.12	0:48	-
90.13	1:09	-
90.14	1:04	Tendon a bit thicker than normal, caudal/distal last suture pass was missed, then Supramid 2/0 was used to "shuttle" the Fiberwire through
90.15	1:04	Superficial cranial drilling: drill bit is broken in the hole. New superficial cranial drill hole made cranially with respect the first one. Broken drill bit left inside the bone because salvaging it would cause too much damage to the tissue
90.16	0:57	-
90.17	1:25	-
90.18	1:08	-
90.19	1:04	-
90.20	1:00	Surface of cranial part of the tendon is covered by a part of the muscle. Shape of tendon is fan-like. Surgeon freed the tissue (tendon/muscle). It could be that sheep bumped each other. This could cause more fibrosis.
90.21	1:02	Tendon is relatively thick
90.22	1:09	-
90.23	0:54	Tendon flatter then usual
90.24	0:59	-

8.7 Macroscopic Evaluation Results

Sheep	Survival (weeks)	Treatment	Hematoma (0 - 1)	Inflammation (0 - 3)	Tendon Visibility (0 - 1)	Fibrosis (0 - 2)	Tendon Thickness (0 - 2)	Tendon tearing (0 - 1)	Gap (0 - 1)	Suture tearing (0 - 1)	Suture cheese wiring (0 -1)	Inflammation at stitch (0 - 3)	Knot security at plate (0 - 2)	Prox bone tunnel widening (0 - 1)	TOTAL (0 - 19)
90.01	6	RI	0	0	0	0	1	0	0	0	0	1	0	0	2
90.02	6	RI	0	0	0	1	1	0	0	0	1	0	0	1	4
90.03	6	RI	0	0	0	1	1	1	1	0	1	1	0	0	6
90.04	6	RI	0	0	0	1	1	0	0	0	0	0	0	0	2
90.05	6	RI	1	2	0	1	1	0	1	0	0	2	0	0	8
90.06	6	RI	0	0	0	1	0	0	0	0	0	2	0	0	3
90.07	13	TI	0	0	0	0	2	0	0	0	0	0	0	0	2
90.08	13	TI	0	0	0	0	1	0	0	0	0	0	0	0	1
90.09	13	TI	0	0	0	0	2	0	0	0	1	0	0	0	3
90.10	13	RI	0	0	0	1	2	0	0	0	0	1	0	1	5
90.11	13	TI	0	0	1	1	2	0	0	0	1	0	0	1	6
90.12	13	TI	0	0	0	0	1	0	0	0	0	0	0	0	1
90.13	13	RI	0	0	0	1	2	0	0	0	1	0	0	0	4
90.14	13	RI	0	0	0	1	2	0	0	0	1	1	0	0	5
90.15	13	RI	0	0	0	2	0	0	0	0	1	2	0	1	6
90.16	13	TI	0	0	0	0	2	0	0	0	0	0	0	0	2
90.17	13	RI	0	0	0	1	2	0	0	0	0	0	0	0	3
90.18	13	RI	0	0	0	1	1	0	0	0	0	0	0	0	2
90.19	6	TI	0	0	0	1	1	0	0	0	1	1	0	1	5
90.20	6	TI	0	0	0	0	1	0	0	0	0	0	0	0	1
90.21	6	TI	0	0	0	0	1	0	0	0	0	0	0	1	2
90.22	6	TI	0	0	0	1	2	0	0	0	0	1	0	0	4
90.23	6	TI	0	0	0	1	1	0	0	0	0	1	0	0	3
90.24	6	TI	1	0	0	1	2	0	0	0	0	1	0	0	5

8.8 Macroscopic Evaluation Comments and Findings

Animal number	Macroscopic Evaluation Comments
90.01	Some adhesion on the superficial muscle on approach (normally after surgery). Very normal healing. Fascia was intact, nicely healed. Plate was fixed, not loosened. A bit of adhesion between deltoid and edge of tendon (normal). Mild fibrosis considered normal after surgery. Whole tendon covered by fibrous sheath, but not too much. Enlargement cranially by 4-5mm. Gap filled with fibrosis tissue. Fibrous sleeve on underside, cut away to visualize gap and sutures. No cheesewiring seen macroscopically.
90.02	Mild fibrosis between the deltoid and infraspinatus. Fibrosis sleeve removed. Plate was a bit looser. Knots were still secure. More hidden in fibrous tissue. Loosening might have occurred more proximally. Callus over screw on caudal side. Tendon thickened. More fibrosis in general everywhere. Additional about 6mm fibrosis caudally. Sutures looser than last time. Deep caudal suture might have cheese wiring. Frizzled ends of tendon. Underside cuff cut off. Proximal bone tunnel widening (cranial and caudal).
90.03	Fibrosis layer on top of tendon area larger than normally seen at this stage. Tendon sleeve thicker. Plate itself looser, covered by fibrous sleeve, not as embedded in the fibrous tissue. More stable. Less fibrosis on plate itself. Less fibrosis between muscles, more adhesions. Markers difficult to find, buried in fibrous tissue with distal caudal steel loop likely "retracted". Cartilage damage noted, reddened. Fibrosis sleeve thicker. Gap filled with fibrous tissue with not much strength. Possible tendon necrosis above the gap, under sutures. Suture cheese wiring suspected.

Animal number	Macroscopic Evaluation Comments
90.04	Plate moderately loose, fibrosis around plate. Tendon looks smooth, more localized fibrosis, compared to the others. Really good in healing. Mild fibrosis on the backside of infraspinatus muscle compared to the others.
90.05	Hematoma between superficial muscle and deltoid muscle. Plate well embedded, less fibrosis around plate, no fibrosis on the plate. Hematoma did not affect the tendon. Fibrotic tissue above the tendon was not white, but darker (orange) and a little sack-like. Inflammation at capsule of hematoma. Cut the fibrosis tissue on the cranial and caudal side of the tendon to make exact measurements (made in every sheep). Not a lot adhesion between backside of infraspinatus and humeral tuberosities. More fibrosis on the backside of infraspinatus. Sutures on backside clearly looking good. Tissue above the gap was changed, possible necrosis. More adhesion on the level of repaired tendon.
90.06	Plate was very firm. Sutures not open. Adhesion between tendon and deltoid muscle (first sheep in which we see that, this is more difficult to prepare). Fibrosis a lot deeper than in the others, in direction of the humeral head. Tendon just a little bit thicker on the bottom (region of humeral head), same in all sheep until yet. A lot of adhesion between humeral head and infraspinatus. "Fibrosis ring" has some muscle in it. Changed tissue above gap (yellowish, lumpy). Cheese wiring difficult to detect on day of sacrifice and on pictures.
90.07	Deltoid muscle attached with some fibrous tissue to tendon. Tendon seemed enlarged. Tendon consistency felt normal. Tendon with glistening surface is coming back, without irregularities. Tendon seemed to have the same alignment, no irregularities, no abnormal color. Sutures cut on the cranial side when intact tendon was released.
90.08	Suture very nicely incorporated. Overall swelling not so notable. A bit of a tail of silicone visible (about 1 mm). Sutures intact. Deltoid fibrous tissue attachments to the tendon are milder.
90.09	No reaction notable. Sutures readily visible. Silicone core coming out a bit at the end (about 1 mm). Deltoid fibrous adhesions to the tendon were visible, notable. Tendon was fibrosed. Tendon had clean, non-adherent edge. Tendon tissue between sutures not as normal as in 90.07 or 90.08, but it still looked fine. A bit cheese wiring on cranial side. Split between healed and unharmed tendon clearly visible.
90.10	Some adhesion from deltoid muscle but tissue retraction milder. Adhesion between deltoid and tendon is strong / tight. Adhesion thicker, so was tendon. Tendon was notably thicker. Fibrous tissue on the underside. Not nice calm tendon tissue. Suture cheesewiring not visible. New tissue did not look mature yet. Bone tunnel proximal a bit widened.
90.11	On the outside, the bump was more prominent. Fibrosis more present. Tendon covered underneath, requiring some blunt dissection. Tissue under suture threads on the underside was better quality. Evidence of previous cheesewiring, healed over. Threads at the end were okay, no popping or opening. Bone tunnel proximal looked widened upon further dissection.
90.12	Less of a fibrous bump. Deltoid easier to detach. Plate well incorporated, firm. Threads around plate were harder (more telling of Dynacord). Not much fibrosis on underside close to the insertion. New tissue a bit pink but nice and structured. No evidence of cheesewiring.
90.13	Deltoid attached to infraspinatus muscle. Difference of tendon could be seen. Moderate fibrosis and cartilaginous. Tendon little bit thicker. Sutures quite lose but intact.
90.14	Deltoid muscle well attached, more than in the other animals. Sutures in fibrous tissue. More fibrosis. A lot more cartilage, especially on healthy part. Clearly thickened on healthy part of tendon quite thin on cut part. Suture was loose.
90.15	Very fibrotic but not severe. Sutures well incorporated. Stitches were loose. Tendon itself was thin, but with cartilage it seemed thicker (much thicker). Hematoma on backside.

Animal number	Macroscopic Evaluation Comments
90.16	Deltoid a bit attached but not much. Plate was not visible upon dissection (a bit lower), nicely incorporated. Tendon was thicker closer to insertion. Tendon looked nice on the underside. Well healed. New tissue looked like tendon. Shiny appearance. No evidence of cheesewiring.
90.17	More adhesive than usual. Deltoid well attached, but not excessively. Plate well incorporated, very firm. A bit more fibrous covering on the underside of tendon. Glimmering of tendon tissue visible. Fibrous sheath over newer tendon tissue. No visible evidence of cheesewiring. Sutures placed higher than usual so not very visible through fibrous sheath.
90.18	Deltoid firmly attached more than usual. There may have been a retraction but was resolved. Plate was a bit loose, but well integrated, not irritated. Fibrous sleeve covering tendon distally. Tendon very firmly attached to bone, more than usual, more fibrous tissue. Not as easy to open "joint" on the underside. Attachment tissue thicker than usual. Callus-like tissue formed on top of healthy part, which made it difficult to open the underside. New tendon tissue felt equal and firm. Cut suture strands to release 7-hole-plate done during preparation at TAT01.07 by mistake. Sample was then handled with extra care so no damage was expected.
90.19	Mild adhesions between Deltoid muscle and infraspinatus muscle. Tendon covered by sleeve, not so shiny. Not much thickening. Fibrosis on the caudal side. Sutures are firm. Might show evidence of cheesewiring, unsure. Fibrous tissue in tunnels, some widening.
90.20	Sack-type formation between tendon and overlaying fascia. Tendon visible and intact. Shiny appearance. Not much adhesion to muscle tissue. Caudal cheesewiring suspected (not conclusive). Difficult to say for sure. No evidence of cheese wiring found after dissection following mechanical testing.
90.21	Mild adhesion. Sutures well incorporated around plate. Plate firm. Some bleeding on the underside and widening of tunnels.
90.22	Threads nicely incorporated at plate. Moderate adhesion of deltoid. Bow on underside larger in volume than usual. Fibrous sleeve with fibers (tendon tissue) underneath. Reddening underneath is new tendon tissue.
90.23	A bit of swelling detected. Adhesion of deltoid is moderate. Tendon was shifted. Caudal muscle ingrown. Sutures well incorporated. Plate nicely fixed. Bow area on the underside was larger than usual. Bow was partially cut away. Little hematoma at cranial suture row. Fibrous tissue was covering, forming a sleeve. Difference between new and normal tendon was visible. During preparation one of the sutures was cut at the insertion.
90.24	Hematoma above (proximal) to the operation site, not next to it. Seemed superficial (above muscles). Some fibrosis. Sutures at plate not readily visible. Under a fibrotic cap, possibly due to hematoma. Plate well incorporated, sutures intact. Tendon thicker (fibrous coverage) possibly due to hematoma. Hematoma at the stitches. New tendon felt good. Fibrous sheath, tendon could be seen underneath.

8.9 Measurement Results

Measurements during surgery

Sheep	Survival (weeks)	Treatment	Prox. Tendon width (mm)	Dist. Tendon width (mm)	Distance between prox. steel loops (mm)	Distance between distal steel loops (mm)	Distance between marking screws (mm)	Distance from caudal screw to prox loop (mm)	Distance from caudal screw to dist loop (mm)	Distance from caudal prox loop to dist loop (mm)	Distance from cranial screw to prox loop (mm)	Distance from cranial screw to dist loop (mm)	Distance from cranial prox loop to dist loop (mm)
90.01	6	RI	24.0	21.0	14.5	17.0	27.5	34.0	19.5	18.5	35.5	14.5	28.0
90.02	6	RI	25.0	22.5	14.0	14.0	29.0	37.5	26.5	14.5	41.0	29.0	15.0
90.03	6	RI	27.0	21.0	11.0	15.0	29.0	38.5	20.0	19.0	35.0	18.5	19.5
90.04	6	RI	27.0	21.0	12.5	12.5	31.0	33.5	19.5	14.0	39.1	21.5	19.0
90.05	6	RI	26.5	21.0	10.5	12.0	26.0	44.0	16.5	26.5	44.0	19.5	33.0
90.06	6	RI	24.0	21.0	13.5	14.5	24.5	39.0	23.5	15.5	36.5	24.5	14.5
90.07	13	TI	24.0	21.0	12.0	15.5	26.0	32.0	21.0	9.5	33.5	21.5	15.5
90.08	13	TI	26.0	21.0	14.0	16.0	27.0	36.5	25.0	13.5	33.5	21.5	15.0
90.09	13	TI	29.0	21.0	12.0	16.0	25.5	31.0	18.5	15.0	37.0	18.0	23.0
90.10	13	RI	28.0	21.0	10.5	10.5	22.0	31.5	18.0	13.0	37.0	23.0	12.0
90.11	13	TI	26.0	21.0	14.0	13.0	27.0	34.0	21.0	12.0	32.5	22.5	13.5
90.12	13	TI	22.0	22.0	10.0	11.0	25.0	30.0	18.5	11.5	35.5	22.0	15.0
90.13	13	RI	27.0	21.0	12.0	10.5	22.5	24.5	13.5	12.0	28.0	16.0	11.5
90.14	13	RI	23.0	21.0	11.0	9.0	20.5	30.1	10.6	16.0	31.0	16.5	16.0
90.15	13	RI	27.5	23.0	14.0	12.5	22.5	35.5	25.0	11.0	32.0	20.5	11.5
90.16	13	TI	28.0	21.0	12.0	11.0	24.5	34.0	20.5	14.5	32.5	20.5	14.5
90.17	13	RI	24.5	21.0	10.0	10.0	25.0	34.0	24.0	8.0	40.0	30.0	9.0
90.18	13	RI	31.0	22.0	11.5	10.0	26.5	34.0	23.0	12.0	37.0	27.0	13.5
90.19	6	TI	26.0	21.0	16.5	13.5	29.5	33.0	25.5	10.5	43.5	30.0	9.5
90.20	6	TI	25.5	22.5	11.0	10.0	25.5	36.5	20.5	15.0	36.0	25.0	12.5
90.21	6	TI	27.0	21.0	14.5	13.0	25.0	35.0	27.0	9.0	37.0	29.0	9.0
90.22	6	TI	23.0	20.5	10.0	11.0	26.0	29.5	19.0	10.0	36.0	25.5	11.5
90.23	6	TI	32.0	25.0	9.0	12.0	25.5	37.0	24.0	29.5	37.0	26.0	15.0
90.24	6	TI	25.0	23.0	14.0	13.0	28.0	40.0	29.0	9.0	37.0	22.5	16.0

Measurements after sacrifice

Sheep	Survival (weeks)	Treatment	Prox. Tendon width (mm)	Dist. Tendon width (mm)	Distance between prox. steel loops (mm)	Distance between distal steel loops (mm)	Distance between marking screws (mm)	Distance from caudal screw to prox loop (mm)	Distance from caudal screw to dist loop (mm)	Distance from caudal prox loop to dist loop (mm)	Distance from cranial screw to prox loop (mm)	Distance from cranial screw to dist loop (mm)	Distance from cranial prox loop to dist loop (mm)
90.01	6	RI	33.5	30.0	18.5	23.0	27.0	36.5	23.0	17.0	37.0	17.5	27.0
90.02	6	RI	34.0	31.0	15.5	16.5	28.0	40.0	31.0	11.0	43.0	32.5	16.0
90.03	6	RI	30.5	35.0	9.0	18.0	28.5	40.0	32.0	11.0	38.0	20.5	18.5
90.04	6	RI	30.0	33.0	14.5	15.0	31.0	35.5	25.0	11.0	37.0	25.0	14.0
90.05	6	RI	26.0	32.0	11.0	20.0	25.0	45.5	24.0	23.0	47.0	21.0	32.0
90.06	6	RI	30.0	33.0	14.0	22.0	25.0	43.0	32.0	11.5	39.0	23.0	19.0
90.07	13	TI	32.0	27.5	18.5	14.0	26.0	33.0	21.0	12.5	36.0	20.0	16.5
90.08	13	TI	26.0	25.0	11.0	14.0	26.5	37.0	29.0	11.0	30.0	22.0	14.5
90.09	13	TI	25.0	28.0	14.0	16.0	26.0	36.0	24.0	11.0	35.0	19.0	26.0
90.10	13	RI	31.0	33.0	13.0	11.0	29.0	41.0	28.0	13.0	42.0	33.0	17.0
90.11	13	TI	33.5	33.0	15.5	11.0	29.0	38.0	27.0	12.0	30.5	25.0	15.5
90.12	13	TI	33.0	28.0	10.0	18.0	25.0	35.0	26.0	11.0	40.0	23.0	18.5
90.13	13	RI	26.0	27.0	14.0	12.0	22.0	31.0	22.0	10.0	35.0	21.0	14.0
90.14	13	RI	27.0	29.0	15.0	12.0	22.0	34.0	26.5	9.0	30.0	16.0	17.0
90.15	13	RI	32.0	30.5	n/a	18.5	23.0	43.5	33.5	12.0	n/a	36.0	n/a
90.16	13	TI	27.0	32.0	10.5	12.0	24.0	33.5	24.0	10.5	33.0	21.0	15.5
90.17	13	RI	26.0	27.0	10.5	12.0	26.0	35.5	30.0	8.0	40.0	29.5	11.5
90.18	13	RI	27.0	25.0	12.0	14.5	27.0	37.0	28.5	11.0	40.5	32.0	12.0
90.19	6	TI	31.0	27.0	17.0	18.0	30.5	36.0	29.0	9.0	43.5	30.5	14.5
90.20	6	TI	28.5	27.5	10.5	13.0	26.0	39.0	31.0	10.0	39.0	27.5	13.5
90.21	6	TI	29.0	29.0	15.0	15.5	25.0	42.0	33.5	9.0	36.5	28.0	11.0
90.22	6	TI	25.0	26.0	11.5	13.5	26.0	34.0	25.0	13.0	38.0	32.0	7.5
90.23	6	TI	28.0	28.0	10.0	17.0	25.0	39.0	30.5	12.0	39.0	29.0	15.0
90.24	6	TI	34.0	33.0	13.5	13.5	27.0	40.0	35.0	9.0	43.0	32.0	14.0

Delta Values

Sheep	Survival (weeks)	Treatment	Prox. Tendon width (mm)	Dist. Tendon width (mm)	Distance between prox. steel loops (mm)	Distance between distal steel loops (mm)	Distance between marking screws (mm)	Distance from caudal screw to prox loop (mm)	Distance from caudal screw to dist loop (mm)	Distance from caudal prox loop to dist loop (mm)	Distance from cranial screw to prox loop (mm)	Distance from cranial screw to dist loop (mm)	Distance from cranial prox loop to dist loop (mm)
90.01	6	RI	9.5	9.0	4.0	6.0	-0.5	2.5	3.5	-1.5	1.5	3.0	-1.0
90.02	6	RI	9.0	8.5	1.5	2.5	-1.0	2.5	4.5	-3.5	2.0	3.5	1.0
90.03	6	RI	3.5	14.0	-2.0	3.0	-0.5	1.5	12.0	-8.0	3.0	2.0	-1.0
90.04	6	RI	3.0	12.0	2.0	2.5	0.0	2.0	5.5	-3.0	-2.1	3.5	-5.0
90.05	6	RI	-0.5	11.0	0.5	8.0	-1.0	1.5	7.5	-3.5	3.0	1.5	-1.0
90.06	6	RI	6.0	12.0	0.5	7.5	0.5	4.0	8.5	-4.0	2.5	-1.5	4.5
90.07	13	TI	8.0	6.5	6.5	-1.5	0.0	1.0	0.0	3.0	2.5	-1.5	1.0
90.08	13	TI	0.0	4.0	-3.0	-2.0	-0.5	0.5	4.0	-2.5	-3.5	0.5	-0.5
90.09	13	TI	-4.0	7.0	2.0	0.0	0.5	5.0	5.5	-4.0	-2.0	1.0	3.0
90.10	13	RI	3.0	12.0	2.5	0.5	7.0	9.5	10.0	0.0	5.0	10.0	5.0
90.11	13	TI	7.5	12.0	1.5	-2.0	2.0	4.0	6.0	0.0	-2.0	2.5	2.0
90.12	13	TI	11.0	6.0	0.0	7.0	0.0	5.0	7.5	-0.5	4.5	1.0	3.5
90.13	13	RI	-1.0	6.0	2.0	1.5	-0.5	6.5	8.5	-2.0	7.0	5.0	2.5
90.14	13	RI	4.0	8.0	4.0	3.0	1.5	3.9	15.9	-7.0	-1.0	-0.5	1.0
90.15	13	RI	4.5	7.5	n/a	6.0	0.5	8.0	8.5	1.0	n/a	15.5	n/a
90.16	13	TI	-1.0	11.0	-1.5	1.0	-0.5	-0.5	3.5	-4.0	0.5	0.5	1.0
90.17	13	RI	1.5	6.0	0.5	2.0	1.0	1.5	6.0	0.0	0.0	-0.5	2.5
90.18	13	RI	-4.0	3.0	0.5	4.5	0.5	3.0	5.5	-1.0	3.5	5.0	-1.5
90.19	6	TI	5.0	6.0	0.5	4.5	1.0	3.0	3.5	-1.5	0.0	0.5	5.0
90.20	6	TI	3.0	5.0	-0.5	3.0	0.5	2.5	10.5	-5.0	3.0	2.5	1.0
90.21	6	TI	2.0	8.0	0.5	2.5	0.0	7.0	6.5	0.0	-0.5	-1.0	2.0
90.22	6	TI	2.0	5.5	1.5	2.5	0.0	4.5	6.0	3.0	2.0	6.5	-4.0
90.23	6	TI	-4.0	3.0	1.0	5.0	-0.5	2.0	6.5	-17.5	2.0	3.0	0.0
90.24	6	TI	9.0	10.0	-0.5	0.5	-1.0	0.0	6.0	0.0	6.0	9.5	-2.0

8.10 Biomechanics Results

Sheep	Survival (weeks)	Treatment	Non-Destructive Apparent Stiffness (N/mm)	Destructive Apparent Stiffness (N/mm)	Ultimate Strength (N)	Yield Point (N)
90.01	6	RI	71	108	1289	1207
90.02	6	RI	47	62	395	267
90.03	6	RI	82	153	984	947
90.04	6	RI	35	86	792	792
90.05	6	RI	61	66	192	136
90.06	6	RI	42	68	204	204
90.07	13	TI	63	163	1087	1070
90.08	13	TI	51	70	783	783
90.09	13	TI	54	107	1767	1517
90.10	13	RI	26	124	1405	1210
90.11	13	TI	28	100	1181	1178
90.12	13	TI	41	120	890	819
90.13	13	RI	68	127	1743	1634
90.14	13	RI	49	135	825	737
90.15	13	RI	36	90	949	815
90.16	13	TI	49	104	960	866
90.17	13	RI	54	101	680	483
90.18	13	RI	45	101	829	772
90.19	6	TI	36	69	516	503
90.20	6	TI	51	71	723	723
90.21	6	TI	34	44	313	251
90.22	6	TI	44	103	822	779
90.23	6	TI	45	82	729	722
90.24	6	TI	39	75	628	588

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10 Curriculum vitae

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